Volume 60 Number 714
June 1987

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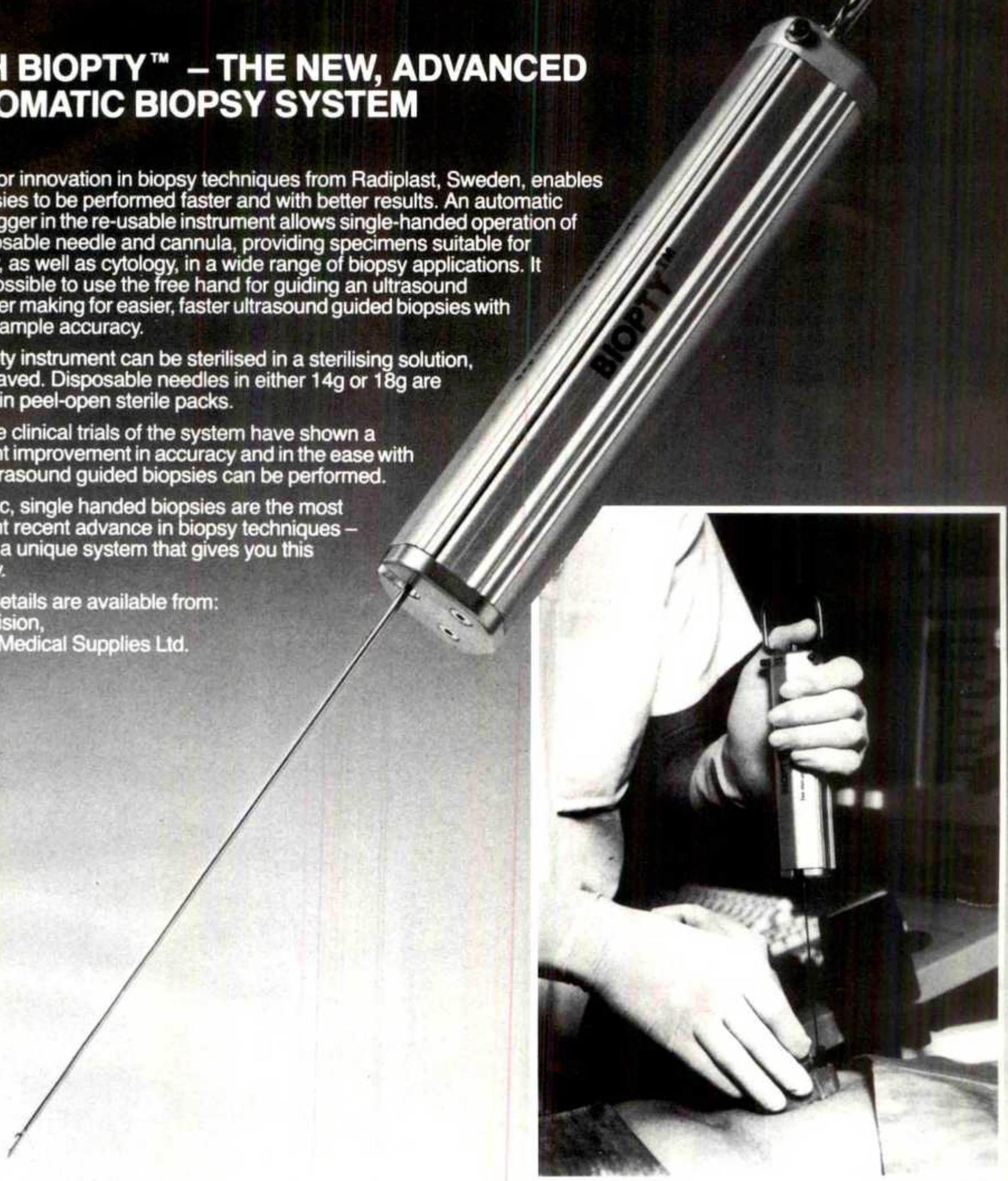

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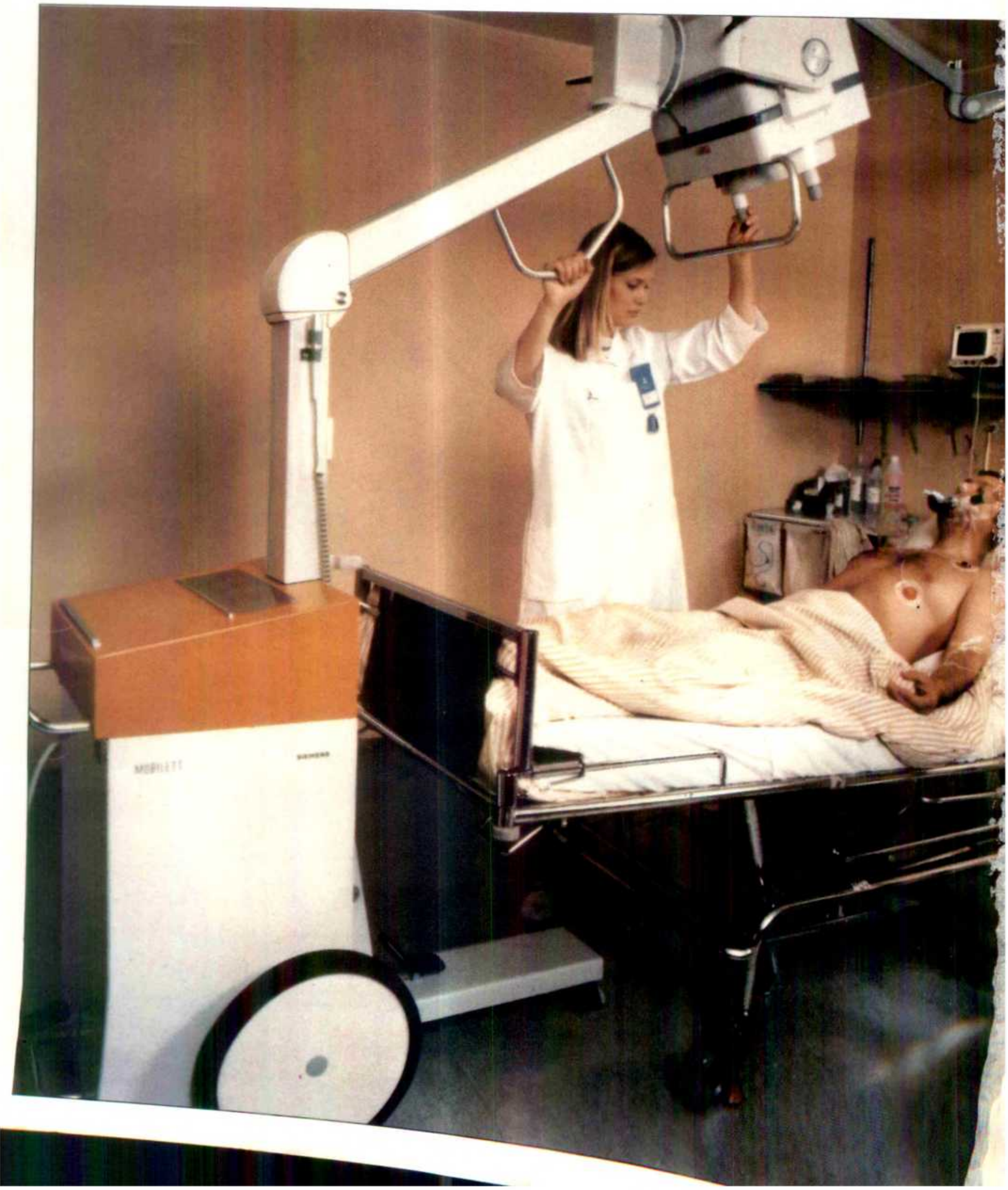

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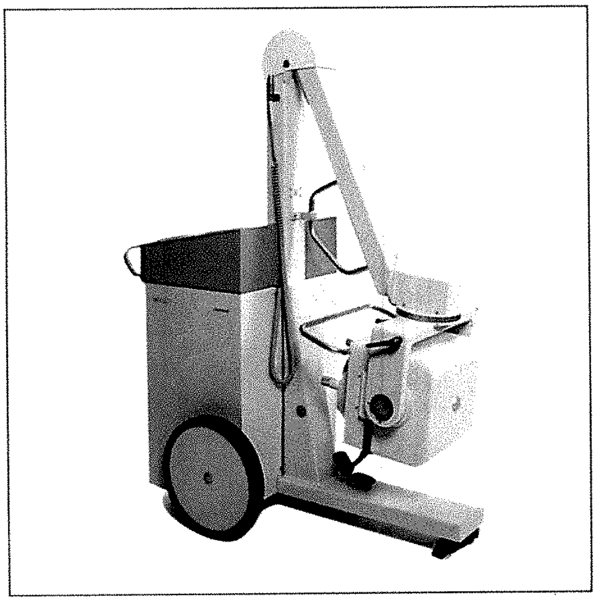

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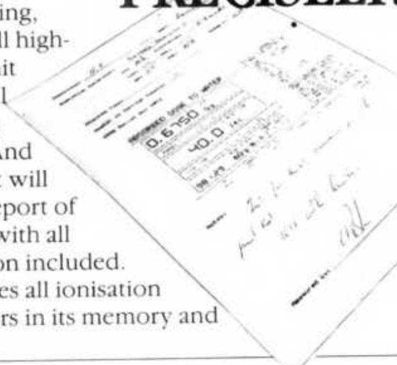

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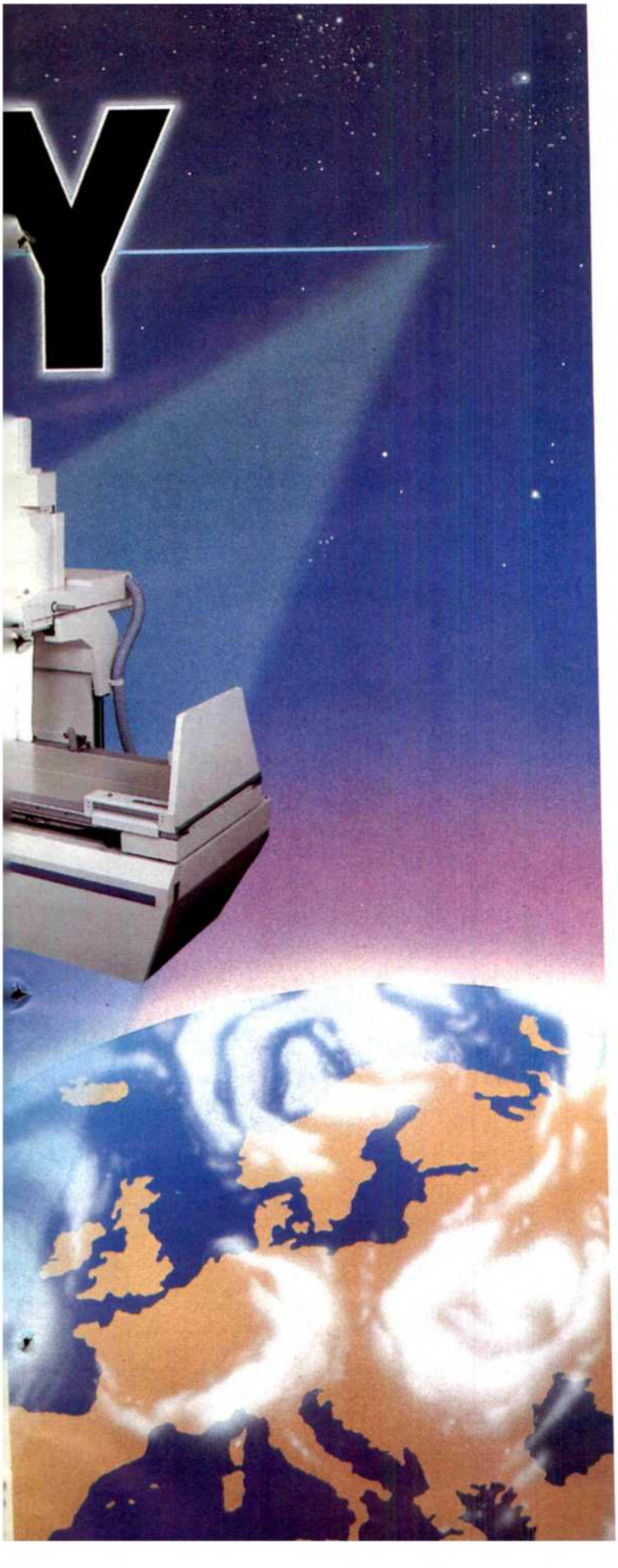

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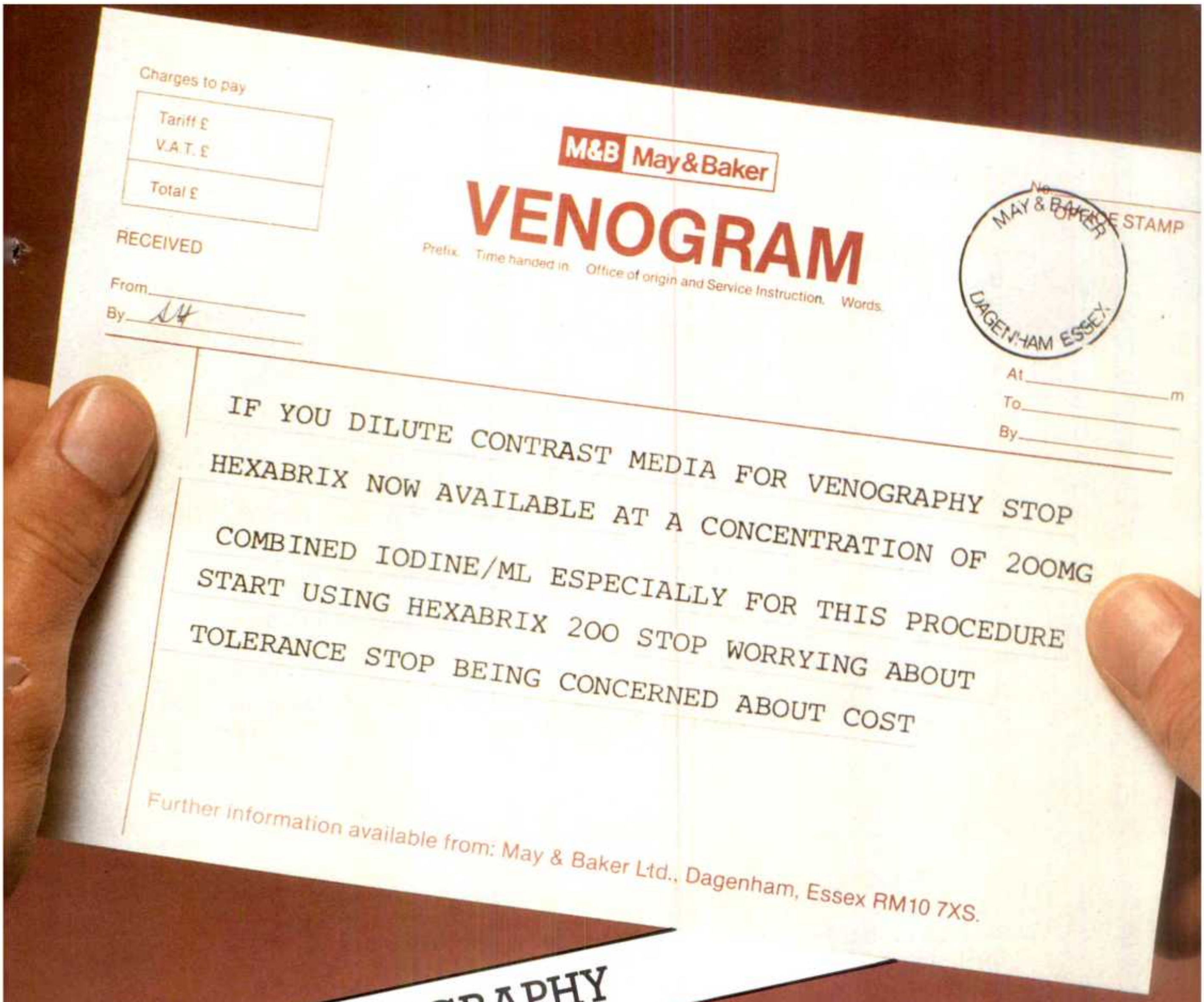

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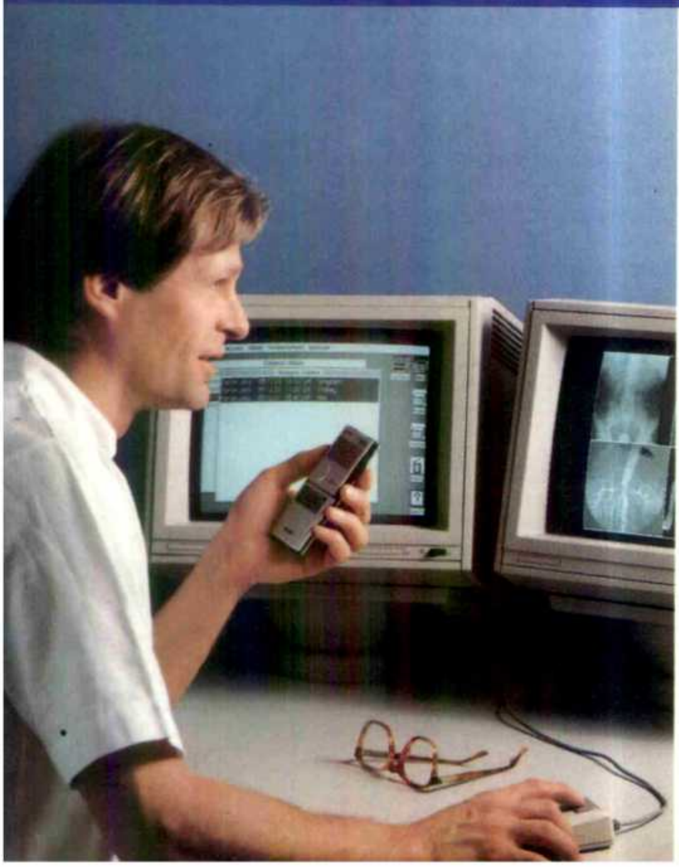

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VOLUME 60 NUMBER 714 JUNE 1987

The British Journal of Radiology

# A new method using ultrasound for measuring femoral anteversion (torsion): technique and reliability

By S. S. Upadhyay, B.Sc., D.M., M.B.B.S., M.S.(Orth.), *T. O'Neil, D.C.R., S.R.N., R. G. Burwell, B.Sc., M.D., F.R.C.S. and †A. Moulton, F.R.C.S.

Queen's Medical Centre, Nottingham NG7 2UH, *Mansfield District General Hospital, Mansfield, Nottinghamshire NG18 1PH and †Harlow Wood Orthopaedic Hospital, Nr Mansfield, Nottinghamshire NG18 4TH

(*Received August 1986*)

ABSTRACT

This paper reports details of a new method using medical ultrasound for measuring femoral anteversion (strictly torsion), and a reliability study of the method separately on each of 10 healthy children and 20 adults. The method involves using a static-image B-mode ultrasound scanner to obtain scans at the hips and knees of the lower limbs. A technique using bone-surface contours is reported for defining, on each hip scan, the head–neck line and, on each knee scan, the transcondylar line By superimposing the transcondylar line on the head–neck line, the angle of femoral anteversion (torsion) was calculated for each limb In the reliability study, scans were obtained three times at both hips and knees of each subject. The femoral anteversion was measured for each limb The intra-observer error was within ±2.3° (95% confidence limits) between scans, which was not statistically significant for the measured anteversion in each of the right and left femora of children and adults separately. To test the validity of the tracing method used to calculate femoral anteversion, one set of scans from the hip and knee of each subject was measured four times; no significant difference was found between tracings for the measurements of femoral anteversion. The ultrasound method is recommended for clinical use We consider the static-image B-mode scanner to be the instrument of choice for measuring femoral anteversion in living subjects

We have recently reported the application of a new method using medical ultrasound for measuring femoral anteversion (strictly torsion) in four samples of subjects with previous posterior traumatic dislocation of the hip, children with Perthes' disease and irritable hips, and healthy children and adults (Upadhyay, 1985; Upadhyay et al, 1985, 1986a, b). This paper reports details of the method and its reliability in an intra-observer error study on healthy children and adults.

## PATIENTS AND METHODS

### *Subjects*

Ten healthy children (six males and four females, age range 3–14 years) and 20 adults (five males and 15 females, age range 19–48 years) had their hips and knees scanned by ultrasound. There were four patients among the adults who had previously dislocated one of their hips and were attending a follow-up clinic at the Mansfield and District General Hospital. One observer (S.S.U.) performed all of the examinations and made calculations from the tracings.

### *Ultrasound equipment*

A standard static-image B-mode ultrasound scanner (Technicare EDP 1000 model) with a calibrated velocity of 1540 m $s^{-1}$ was used. A 5 MHz transducer with a face diameter of 13 mm was used in most cases in this study. In younger children where less penetration was required a 7.5 MHz transducer was used.

### *Technique and method of recording the scans*

The subjects were scanned lying supine on an ordinary table or trolley, with both limbs placed in neutral rotation and held with a foot clamp to prevent any rotation during the procedure. Skin-to-probe contact was made using Aquasonic gel (Scientific and Industrial Equipment Ltd). Each leg was scanned at two levels to obtain cross-sections: one at the greater trochanter of the femur and the other in the knee region. The tip of the greater trochanter is palpated and the probe placed 1–2.5 cm distal to this landmark, over the front of the greater trochanter, taking care not to scan distal to its base (Upadhyay, 1985). If difficulty is found in locating the tip of the greater trochanter, the probe can be used to determine the base of greater trochanter and the scan obtained just proximal to it.

To obtain the hip scan, scanning is started at the trochanter and the probe is moved supero-medially towards the femoral head until the shape of the head, neck and trochanteric region of the femur can be easily recognised as a continuous line on the television monitor (Fig. 1).

At the knee, the probe is positioned just distal to the patella in the midline and directed upwards at an angle of approximately 45° to the horizontal. To obtain the knee scan, a clear picture of the patellar surface of the femur is created, after which the probe is moved around each side of the joint in an arc about 2 cm proximal to the joint line (Fig. 2). The ultrasound images of the hip and knee displayed on the television monitor were

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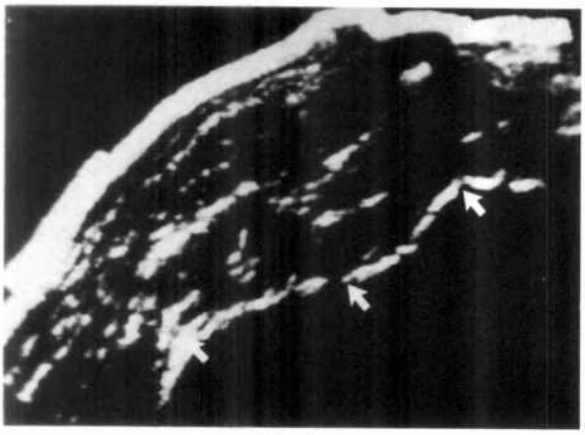

Fig. 1.

Ultrasound scan at the hip in a living subject. The arrows indicate, from left to right, the anterior surfaces of the greater trochanter, neck and head of the femur.

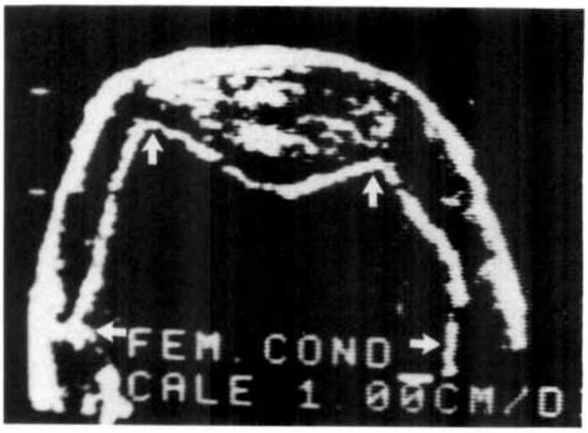

FIG. 2.

Ultrasound scan at the knee in a living subject. Note the patellar groove of the lower end of the femur, the femoral condyles and the patella. The arrows show the anterior projections of the femur condyles (above) and the widest flare of each condyle (below).

recorded on films from a multi-image recorder, with six scans on each film.

*Calculation of femoral anteversion angle*

Each film was placed on a viewing box, to the glass of which was attached a cellulose acetate transparency bearing vertical and horizontal parallel lines. A sheet of tracing paper was attached by clips to the film and its corners marked. The criteria used to determine the lines at hip and knee from which to measure anteversion were as follows (Fig. 3). On the hip scan, a line was drawn on the tracing paper joining the most anterior parts of the trochanter and of the femoral head: this was taken as the "femoral head–neck" line. The knee scan was positioned between parallel lines in a neutral position. Two midpoints were marked on the tracing paper: one on a horizontal line drawn between the most anterior projections of the femoral condyles, and the other between the widest flares of the femoral condyles. The "transcondylar line" was then drawn at right angles to an anteroposterior line connecting the two midpoints. The vertical line (anteroposterior line connecting the two midpoints on the knee tracing) was placed directly over a vertical line on the cellulose acetate transparency; a horizontal line on the transparency is used to draw a horizontal line on the tracing paper beneath the head–neck line to create the angle of femoral anteversion; this is measured to the nearest 0.5° using a protractor.

*Reliability*

*Scans and measurement of tracings*. In each of the 10 children, lying supine, a set of scans was obtained sequentially of the right hip, right knee, left hip and left knee; this was repeated three times in the same order.

In each of the 20 adults, one set of scans was obtained in a similar sequence. After an interval of 6–12 months, the subjects returned to hospital for a repeat examination and two sets of scans were obtained of both hips and knees. Thus, for each adult a total of three sets of scans was also obtained.

*Measurement of tracings*. The first set of scans from

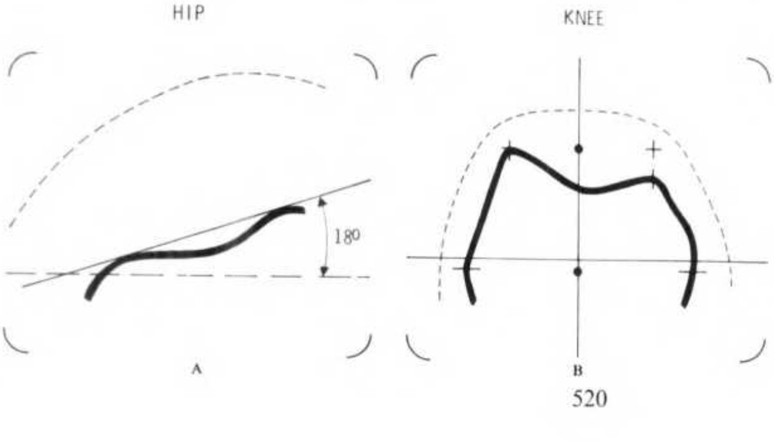

FIG. 3.

Diagram to show the datum points used to draw (A) at the hip, the femoral head–neck line, and (B) at the knee, the transcondylar line of the femur.

each hip and knee of the 10 children and the 20 adults was measured four times using the tracing technique to establish the reliability of the latter separately from the error of the scans for measuring femoral anteversion.

### *Statistical analyses*

Separate statistical analyses were performed for right hips and left hips and also separately for the children and adults.

A two-way analysis of variance was used (Snedecor & Cochran, 1980). The residual mean square is used to calculate the pooled standard deviation from which the 95% confidence limits of the method was calculated for, firstly, the overall method (*i.e.* scans and tracings together) and, secondly, the measurement of the tracings.

## RESULTS

### *Scans and measurement of tracings*

The reliability of findings for the ultrasound method (scans and tracings) for measuring femoral anteversion with respect to the right hip of 10 children is given in Table I. It is seen that 95% confidence limits for the method is ±2.3°. This method of statistical analysis is used to create the findings shown in Table II.

TABLE I

RELIABILITY OF ONE OBSERVER (S.S.U.), USING THE ULTRASOUND METHOD FOR MEASURING FEMORAL ANTEVERSION: FINDINGS FROM THREE SCANS OF THE RIGHT HIPS FOR EACH OF 10 CHILDREN (ANALYSIS OF VARIANCE)

| Source of variation | Sums of squares | Degrees of freedom | Mean squares | F-ratios |
|---|---|---|---|---|
| Scans | 8.07 | 2 | 4.03 | 2.95 |
| Children | 2176.7 | 9 | 241.90 | 176.97 |
| Residual | 24.60 | 18 | 1.37 | |
| Total | 2209.37 | 29 | | |

Pooled SD = $\sqrt{1.37}$ = 1.17. Therefore 95% confidence limits = 1.17 × 2 = ±2.3°

In Table II it is seen that the accuracy of the ultrasound method is similar in children and adults (right and left hips) and is ±1.7° to ±2.3° (95% confidence limits). There is no statistically significant difference between the three sets of scans separately for the children and adults (F-ratios).

### *Measurement of tracings*

The reliability of measuring femoral anteversion by the tracing technique is shown in Table III. There is no significant difference between the reading of femoral anteversion measured four times for each subject, the results of which are shown separately for children and adults (right and left hips); the accuracy of the tracing technique is from ±1.6° to ±2.2° (95% confidence limits).

## DISCUSSION

We first evaluated the ultrasound method to measure femoral anteversion on 30 dried femora (Moulton & Upadhyay, 1982). The results obtained were closely similar to those found using a protractor to measure anteversion in the same bones. In a subsequent statistical analysis of data from 37 dried femora in which femoral anteversion was measured by ultrasound and by a new mechanical method, no significant difference for the methods was revealed (Upadhyay, 1985). Further laboratory work showed that in obtaining an image of the head–neck region of the femur it was important that the probe should be placed at or just proximal to the base of the greater trochanter, a structure which can be readily identified by ultrasound in living subjects (Upadhyay et al, 1987).

Recently, two groups of workers have measured femoral anteversion on dried femora using different ultrasound methods. Zarate et al (1983) used a real-time ultrasound method with a spirit level on the probe

TABLE II

RELIABILITY OF ONE OBSERVER (S.S.U.), USING THE ULTRASOUND METHOD FOR MEASURING FEMORAL ANTEVERSION IN CHILDREN AND ADULTS: FINDINGS FROM THREE SCANS OF EACH HIP FOR EACH SUBJECT (ANALYSIS OF VARIANCE)

| Subjects | Hips | Pooled SD | F-ratios between scans (degrees of freedom) | $p$ | 95% confidence limits of the ultrasound method |
|---|---|---|---|---|---|
| Children ($n$ = 10) | Right | ±1.17° | 2.95<br>(2,18) | NS | ±2.3° |
| | Left | ±1.06° | 2.25<br>(2,18) | NS | ±2.1° |
| Adults ($n$ = 20) | Right | ±0.84° | 0.02<br>(2,38) | NS | ±1.7° |
| | Left | ±1.10° | 0.42<br>(2,38) | NS | ±2.2° |

NS = not significant.

TABLE III

RELIABILITY OF ONE OBSERVER (S.S.U.), USING THE ULTRASOUND METHOD FOR MEASURING FEMORAL ANTEVERSION IN CHILDREN AND ADULTS. FINDINGS FROM FOUR TRACINGS OF ONE SCAN AT THE RIGHT AND LEFT HIPS FOR EACH SUBJECT (ANALYSIS OF VARIANCE)

| Subjects | Hips | Pooled SD | F-ratio between measurements on tracings (degrees of freedom) | $p$ | 95% confidence limits of the measurements on tracings |
|---|---|---|---|---|---|
| Children ($n$ = 10) | Right | ±1.10° | 0.33<br>(3,27) | NS | ±2.2° |
| | Left | ±0.86° | 0.40<br>(3,27) | NS | ±1.7° |
| Adults ($n$ = 20) | Right | ±0.78° | 0.08<br>(3,57) | NS | ±1.6° |
| | Left | ±0.83° | 0.50<br>(3,57) | NS | ±1.7° |

NS = not significant.

so as to place the source of the ultrasound in the horizontal plane. Their method differs from ours in three respects: first, in the dried bone the scan measurements were obtained solely at the hip; secondly, they used a real-time scanner; and thirdly, the use of a "tubercle–neck" line rather than a "head–neck" line.

Phillips et al (1985) used a real-time sector-scanner with 3 MHz transducer to evaluate its reliability for measuring femoral anteversion on one dried femur and concluded that real-time ultrasound could measure anteversion of less than 40° at an acceptable level of accuracy. The intra-observer error was stated to be ±4.1° for a single observer (reading the same angle twice and expressed as a standard deviation). The difference between observers was found to be statistically significant. The method differs from ours in that measurements were obtained solely at the hip, it includes error due to any asymmetry of the femoral condyles in the sagittal plane of the bone, and, lastly, a real-time sector-scanner can only demonstrate a limited section of the required image. This is in contrast to the static-image B-mode scanner, which creates the required image of the femoral head, neck and the greater trochanter and may be better suited to measure femoral anteversion than a real-time sector-scanner.

Our validation of the ultrasound method for measuring femoral anteversion on dried femora led us to apply it to living subjects, for whom reliability findings were essential. The ultrasound method creates an image of the upper end of the femur on which a head–neck line is readily drawn. At the hip, experience with the method facilitates the rapid creation of an acceptable image. At the knee, it is technically easier to obtain a satisfactory image. The datum points which we use at the hip to create the head–neck line strictly should be termed the "head–trochanteric" line, but the femoral tubercle on the front of the greater trochanter (Breathnach, 1958) is not always seen in the images. The use of the femoral head for one datum point implies that the "femoral anteversion" which we measure is a product of the position of the femoral head on the neck (which may not be centred) as well as the torsion within the neck and shaft of the femur (Kingsley & Olmsted, 1948), and the method is inapplicable to the deformed femoral head.

At the knee, the datum points which we now use to obtain the transcondylar line were modified from those of Weiner et al (1978); they used computed tomograms of the knee and drew a "diacondylar" line connecting the two points at the widest flare of the condyles. Our modification overcomes error caused by rotation of the limb and by any anatomical variation of the femoral condylar flare by using, in addition, the anterior midpoint between the femoral condyles.

Our reliability findings show that there was no significant difference for measuring femoral anteversion between the same subjects scanned by one observer on three occasions. Moreover, there was no significant difference between images traced and measured four times to calculate femoral anteversion. The intra-observer reliability for measuring femoral anteversion was found to be between ±1.7° and 2.3° (95% confidence limits, Table II).

Radiological methods used for measuring femoral anteversion include fluoroscopic, biplanar and axial techniques (Brouwer, 1981, Harris, 1983, Upadhyay, 1985). A technique using lateral radiographs had an accuracy of ±10° in routine practice (Ryder & Crane, 1953).

In a theoretical study of a conventional biplanar radiological method for determining femoral anteversion, Henriksson (1980) concluded that the accuracy of the method had a standard deviation of ±5°.

Ruby et al (1979), using one femur with a subtrochanteric osteotomy to alter anteversion, compared three radiographic methods for measuring femoral anteversion. The range of error overall was from −5° to +9°. These workers also discussed the dose of X radiation to which the child is exposed in such attempts to measure the femoral anteversion, and ultrasound offers the possibility of screening examinations without known risk.

In recent years, computed tomographic methods for measuring femoral anteversion in patients have been reported (Reikeras et al, 1983) and it is concluded that the method has a deviation of $0 \pm 4.5°$.

### COMMENT

Our findings show that the ultrasound method using a static-image B-mode scanner for measuring femoral anteversion is reliable and accurate when used by one observer. The technique is simple, easily learned and believed not to have any harmful effect on the subject, making it of potential value in screening procedures. The static-image B-mode scanner is considered to be superior to the real-time scanner for measuring femoral anteversion, firstly, because the image of the bone is better and, secondly, because the use of a transcondylar plane at the lower end of the femur eliminates errors due to any asymmetry of the condyles in the sagittal plane of the bone. We consider it to be the method of choice for measuring femoral anteversion, provided that the femoral head is intact and not deformed.

### ACKNOWLEDGMENTS

We would like to thank the National Fund for Research into Crippling Diseases for help in financing this work, Mrs H. Cobb and Mrs A Edwards of the Ultrasound Department at Mansfield and District General Hospital for their help in this study, Mr G. Lythe, Medical Artist in the Audiovisual Department, Professor R. E. Coupland for some facilities and Mrs A. Clarke for secretarial help

### NOTE ADDED IN PROOF

Since this paper was submitted for publication, Berman et al (1987) have compared CT with an ultrasound method for measuring femoral anteversion. Their ultrasound method was based on the work of Moulton and Upadhyay (1982) and not the method used in our subsequent work (Upadhyay et al, 1985, 1986a, b) and herein described.

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# Book reviews

*Sectional Human Anatomy*. By Man-Chung Han and Chu-Wan Kim, pp viii+224, 1985 (Ilchokak, Seoul; Igaku-Shoin, Tokyo), £55 25.

ISBN 0-89640-118-9 (New York)
4-260-14118-X (Tokyo)

As stated in the preface of this book, with the advent of new diagnostic modalities, including ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI), there is a growing demand for atlases which display the human body in multidirectional section. This atlas, produced by Korean radiologists Han and Kim, makes a valiant effort to correlate photographed gross sectional anatomy directly with CT and MRI illustrations.

The atlas, which is of a high editorial standard, is in four parts, the first dealing with brain, head and neck (transverse and coronal sections), the second with the chest (transverse and sagittal sections) and the third with the abdomen and pelvis (transverse and sagittal sections) Where there are transverse and coronal sections, cadaveric sections are compared directly with CT images. Sagittal tissue sections are included of chest and abdomen in Parts 2 and 3, which can be compared with corresponding MRI images in Part 4. The latter deals exclusively with MRI of regions dealt with in Parts 1 to 3 and also includes transverse and coronal sections, although fewer MRI images are displayed compared with gross anatomy and CT sections.

Cadaveric section preparation, fixation and presentation is professional and photography excellent Labelling is mainly accurate and detailed although the use of dyes in certain sections to accentuate vascular patterns and extravascular potential spaces is excessive and inconsistent within a single specimen Unfortunately certain cadaveric sections do not completely correspond with the accompanying CT section, although one can understand the technical difficulties that this task imposes More importantly, it is a pity that the section on MRI is entirely separate from the other two modalities, precluding direct comparison of all three, and in particular comparison of MRI with sagittal sections of thorax and abdomen. The MRI images are of rather poor quality when compared with images obtainable on more recent machines operating at stronger magnetic field strengths.

This atlas is aimed at the radiologist in pursuit of higher professional qualifications and to this end will be considered a useful addition to current teaching aids, although at £55 it is by no means inexpensive. It may be useful for radiographers and anatomy students as a reference book bearing in mind the greater emphasis being placed upon the study of cross-sectional anatomy. There is, however, no explanatory text to coincide with each section displayed and interpretation of sections and images does require a reasonable degree of anatomical knowledge.

D I. LEWIS-JONES

*Nuclear Techniques in Diagnostic Medicine*. Ed. by P P. van Rijk, pp. x+527, 1986 (Martinus Nijhoff Publishers, Dordrecht), £107 95

ISBN 0-89838-744-2

This volume follows a familiar pattern for textbooks of nuclear medicine, in that the first third is devoted to basic science—physics, imaging techniques, radiopharmaceuticals, radiation dosimetry and computing—and the remaining two-thirds discusses the application of these techniques to different organ systems. There is a healthy emphasis on the principles underlying the techniques, with good discussions of the physiology involved in many cases, for example bone and lung

The 20 authors are drawn from many different centres in Europe and the USA. English is clearly not the first language of many of them; the syntax is distinctly quaint in places and many spelling mistakes have been missed in editing. There is considerable variation in presentation from chapter to chapter In some cases, notably bone, there is no discussion whatsoever of the clinical application of the techniques. There is also some repetition of material; the chapter on the thyroid repeats material on instrumentation, radiopharmaceuticals and physics The illustrations are generally good, although Fig. 6 on p. 395 is upside down and Fig 3 on p. 425 is on its side. Arrows indicating points of interest could be more widely used. There are extensive references following each chapter, although some of these are to techniques which are now obsolete (who would now use $^{131}$I MAA or a rectilinear scanner for lung imaging?).

There is much valuable information and many stimulating ideas, but it is difficult to suggest groups of readers to whom the book can be recommended unreservedly. The preface claims that it will be of interest to clinicians of various specialties and physicians in training as well as diagnostic professionals. In fact there is far too little discussion of clinical applications for the book to be of much value to the general clinician, who would also find the early chapters somewhat intimidating It would be useful for the nuclear medicine specialist in training, but it does not contain enough depth or detail to be his only textbook. Technicians and radiographers would also find the book of interest.

E. P. WRAIGHT

1987, *The British Journal of Radiology*, 60, 525–529 JUNE 1987

# Changes in transplanted kidney volume measured by ultrasound

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*(Received June 1986 and in final form November 1986)*

## ABSTRACT

A simple ultrasonic method was used for measuring transplanted kidney volume in 29 patients. Five of these patients developed diabetes mellitus and six women became pregnant following transplantation. Serial measurements were performed over periods of 6–12 months after transplantation. The kidney volume became stable 6 months after transplantation and this volume correlated positively with the renal function Renal hypertrophy was noted in those transplant patients who developed diabetes mellitus following transplantation and this hypertrophy was associated with improvement in graft function. Transplant volume also rose in acute rejection and returned to normal after appropriate treatment During pregnancy following transplantation, the transplant volume increased early in pregnancy to return to normal before delivery This volume increase was also associated with graft function improvement.

Renal hypertrophy associated with unilateral nephrectomy (Brenner & Rector, 1981), early diabetes mellitus (Christiansen et al, 1982) and pregnancy (Bailey & Rolleston, 1971) is well recognised. Kidney atrophy is a well known feature of chronic renal failure.

Native kidney volume determined by ultrasound has been described previously (Rasmussen et al, 1978; Hricak & Lieto, 1983). We used a similar and simplified ultrasonic method for measuring the kidney volume and applied this method to renal transplants.

The transplant volume has previously been described only during acute rejection episodes (Frick et al, 1981) and during the first week of transplantation (Hricak et al, 1981). To our knowledge, this is the only study that describes the natural history of the transplanted kidney volume over a long period of time and describes also for the first time the transplant kidney volume during pregnancy and diabetes mellitus complicating renal transplantation.

## METHODS

The transplant volume was estimated using a modified version of that described by Hricak & Lieto (1983) and Rasmussen et al (1978) using a B-scanner SDU 7000 (Philips). The longitudinal axis of the transplant was determined. Perpendicular to this axis, Polaroid pictures were taken of each transverse section at 1 cm intervals, using one-to-one magnification. The outline of the transplant on each transverse section was cut out. All the cuts were weighed together on a precision balance. To find the relationship between the weight of the transverse cuts and the transplant volume, we scanned transplants which were scheduled for transplant nephrectomy. The actual transplant volume was measured by water displacement after the surgery and it was found that 1 g of Polaroid weight was equivalent to 66.6 ml. Consequently, the volume was obtained by multiplying the weight of the Polaroid obtained by 66.6 The reproducibility of the method was within ±1.5%. However, it should be emphasised that it was the change in volume and not the actual volume of the transplant that was important in this study

Transplant volume was measured by ultrasound at regular intervals following transplantation, the last volume being taken 6–12 months after transplantation and was referred to as the final volume. In pregnant women, transplant volume measurements were taken at regular intervals and the patients entered the protocol at different stages of their pregnancies.

The renal function was monitored at the same time by estimation of serum creatinine and creatinine clearance Creatinine measurements were done using Technicon (Jaffe's picric acid).

## PATIENTS

A total of 29 patients were studied between September 1983 and December 1984. They were divided into two groups.

*Group 1* consisted of 23 patients, 15 of whom received a live renal transplant from a relative and the remainder a cadaveric transplant. Fifteen patients were treated with azathioprine and the remaining eight with cyclosporin A. Five patients developed diabetes mellitus following transplantation. All patients were also receiving prednisolone.

*Group 2* consisted of six women who had seven pregnancies between them following transplantation. Four of these patients received a live renal transplant from a relative and two received a cadaveric transplant. All the patients were treated with azathioprine and prednisolone

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## RESULTS

Figure 1 shows the final volume of transplanted kidneys in 23 patients (including five diabetics) 6–12 months after transplantation. The serial measurements of the transplant volume showed that this volume remained stable after the sixth month after transplantation This final volume (corrected to body surface area of 1.73 $m^2$) positively correlated with creatinine clearance ($p < 0.01$ using Student's $t$-test). This figure shows also that the chronically failing transplants were associated with small volume.

Compared with non-diabetic patients, diabetic patients tended to have bigger than average final volume (mean volume was found to be 348.4 ml per 1.73 $m^2$ for the diabetics and 261 ml per 1.73 $m^2$ for non-diabetics, $p < 0.02$); and they tended to have better renal function ($p < 0.04$ for creatinine clearance using Student's $t$-test).

During the period of the study, 16 sudden rises in the transplant volume were witnessed using ultrasound measurements and were associated with episodes of acute rejection and deterioration in renal function. The

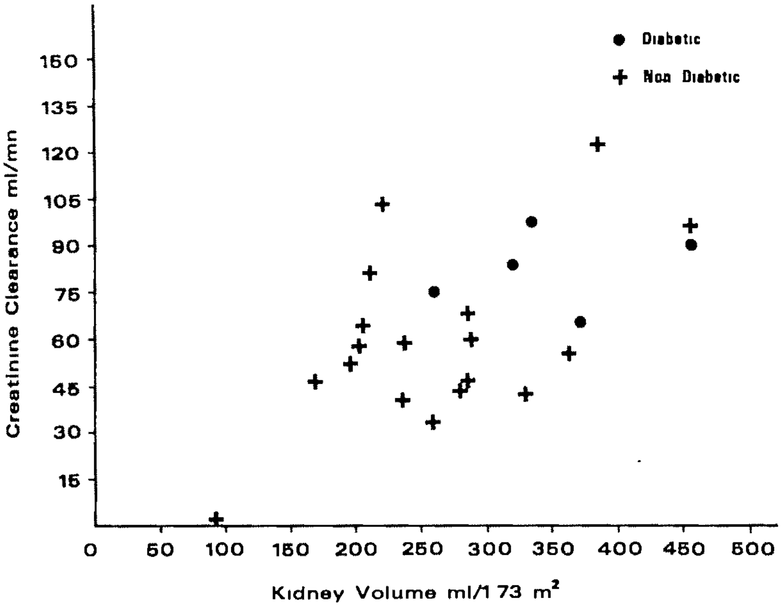

FIG 1

The "final" transplant kidney volume in 23 patients and its relationship to creatinine clearance ($p < 0.01$).

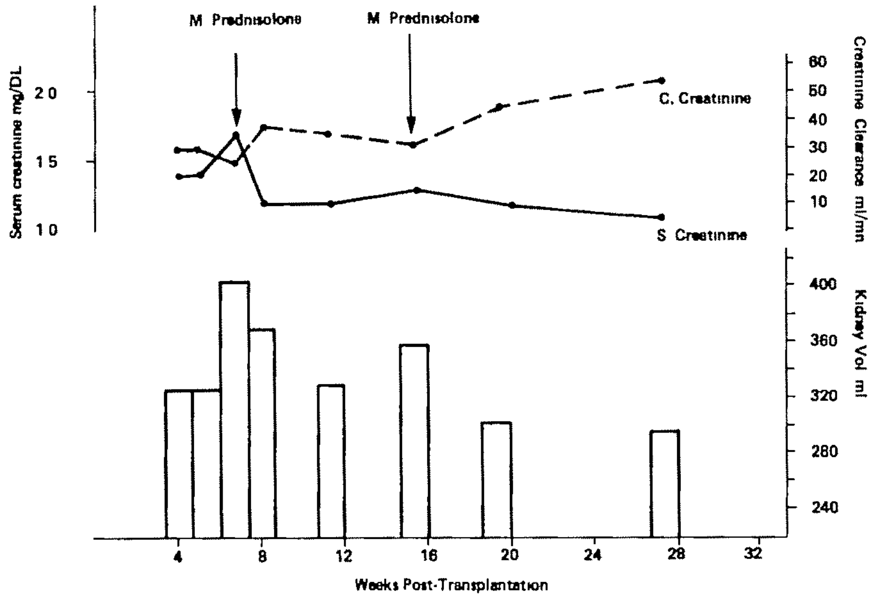

FIG 2

An example of changes in transplant volume (columns) in a transplant patient and its relationship to serum creatinine (solid line) and creatinine clearance (interrupted line).

transplant volume increased rapidly by 10–25% of the previous recorded volume and this increase in volume was completely reversed with return to previous levels after adequate antirejection treatment. In a few cases, routine ultrasound volume measurement showed an increase in the volume of the transplant a few days before the actual deterioration in the renal function, as documented with plasma creatinine level and creatinine clearance.

Figure 2 illustrates the typical course of the transplant volume changes in a non-diabetic patient. The first measurement of the kidney volume was done 4 weeks after transplantation and was found to be 325 ml. Around the seventh week there was a sudden rise in serum creatinine and a drop in creatinine clearance. The transplant volume suddenly rose to about 400 ml. After treatment with methylprednisolone there was a simultaneous improvement in renal function and a reduction in transplant volume, which returned to previous levels.

Another mild episode was recorded around the 16th week. Finally, the transplant volume stabilised around 295 ml as from the 28th week after transplantation.

Figure 3 shows a typical course of volume changes in the transplant of a patient who developed diabetes mellitus following transplantation. The first measurement was done 1 week after transplantation and the volume obtained was 228 ml. The second volume measurement was done at the fourth week on the occasion of a rise in creatinine and the kidney volume had increased to 290 ml. This acute rejection was not treated adequately and the patient experienced a further deterioration in renal function with a rise of serum creatinine and a further rise in transplant volume. This acute rejection was finally treated with methylprednisolone and the transplant volume decreased significantly to reach 240 ml. In the ninth week after transplantation the patient developed diabetes mellitus and the transplant volume started to increase gradually to reach a final volume of 375 ml. During the same period, the renal function improved.

Figure 4 illustrates the changes in transplant volume occurring during pregnancy. The transplant volumes are given in absolute values and have not been correlated to body surface area. Seven pregnancies occurred in six patients. They are represented on two graphs for the convenience of illustration. In Fig. 4B the top two lines represent the volume changes in two consecutive pregnancies in the same patient. The patients entered the protocol at different stages of their pregnancies. Generally, the transplant volume increased in size to a maximum between the 20th and 30th week of pregnancy and then started to decline before delivery and returned to pre-pregnancy size after delivery. The average increase in size of the transplant was found to be about 25% compared to the volume measured at early pregnancy or compared to post-delivery volume. A variable degree of renal function improvement was associated with the transplant volume increase during pregnancy as measured by serum creatinine levels and creatinine clearance. However, no positive correlation was found between volume increase and renal function during pregnancy, the sample being too small. In one patient, represented in the lowest line in Fig. 4B, the changes in transplant volume were minimal. On ultrasonic scanning of these patients we noticed the absence of ureteric or calyceal dilatation during pregnancy.

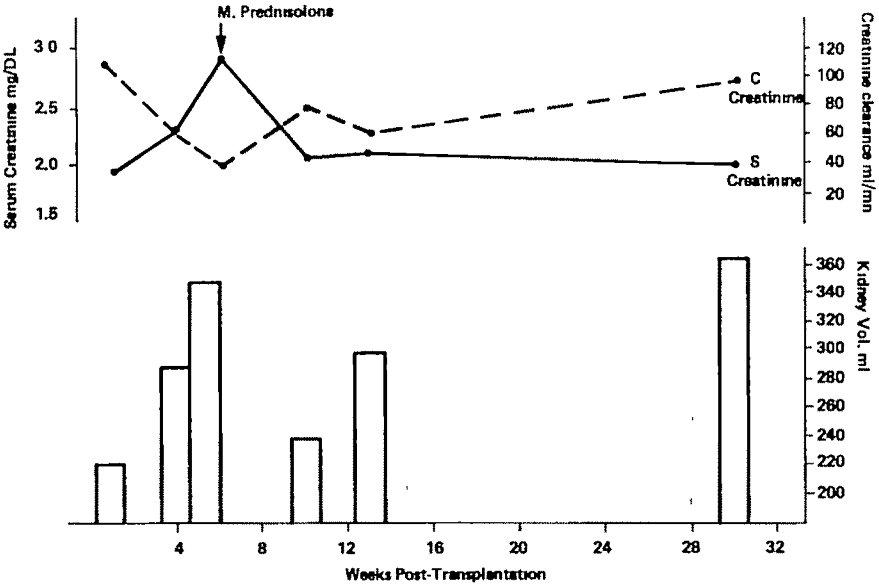

Fig. 3.

An example of changes in transplant volume (columns) in a transplant patient who developed diabetes mellitus at the ninth week after transplantation and its relationship to serum creatinine (solid line) and creatinine clearance (interrupted line).

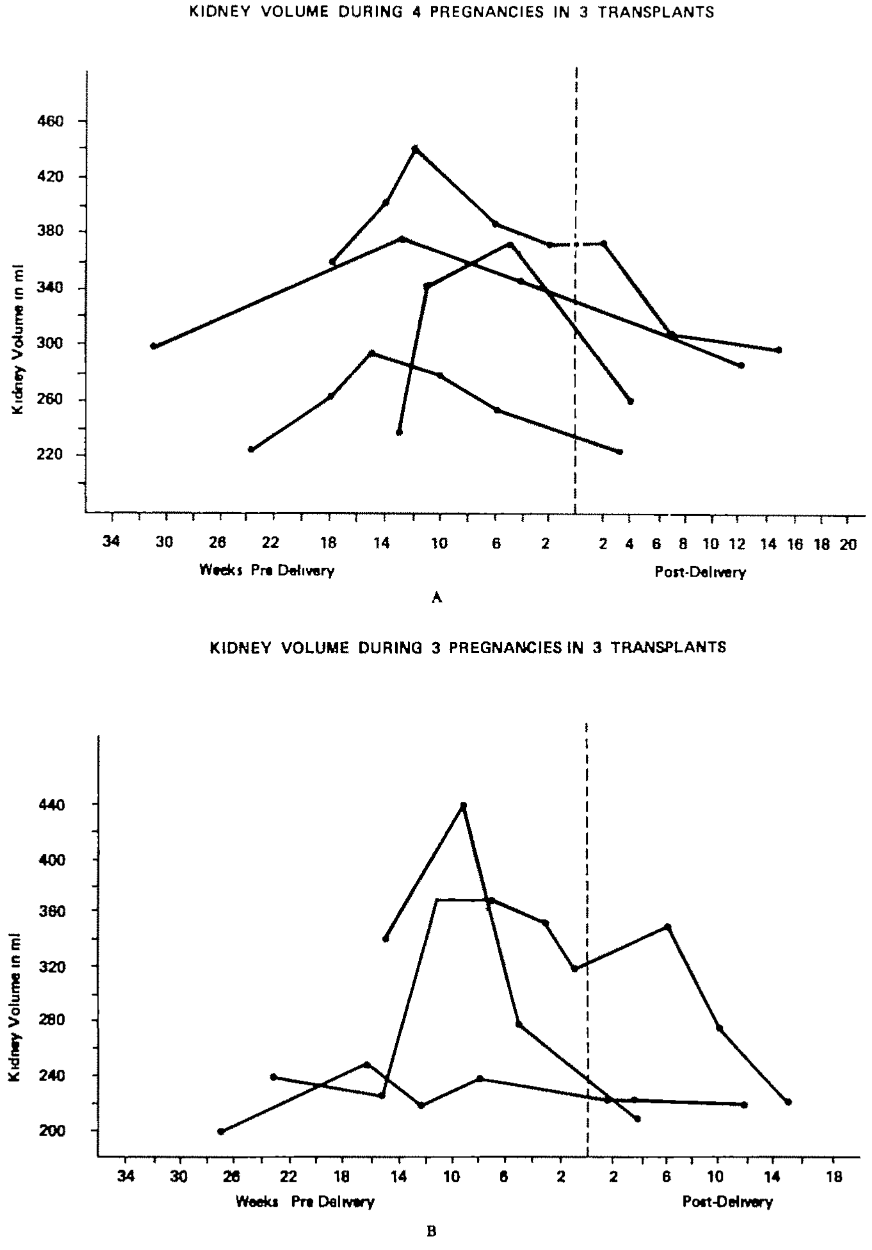

Fig. 4.

(a, b) Changes in transplant kidney volume in seven pregnancies occurring in six women

## Discussion

Earlier studies have described the kidney graft volume changes during the first weeks after transplantation (Hricak et al, 1981), and during rejection episodes (Frick et al, 1981). Using this simple and reproducible ultrasonic method for transplant volume measurement, we were able to describe the volume changes occurring after transplantation in a number of different clinical situations. However, other methods of similar simplicity can be used (Hricak & Lieto, 1983). Most of our measurements were started in the second week following transplantation and so we cannot confirm the early transplant volume increase mentioned by some authors (Hricak et al, 1981). However, we confirm the earlier findings concerning the increase in transplant volume in acute rejection (Frick et al, 1981). We found that the transplant volume increased rapidly by 10–25%, depending on the time of measurement and the severity of rejection. It was also noticed that the volume increase was associated with the classical ultrasonic signs of rejection, *i.e.* cortico-medullary differentiation loss and prominence of pyramids (Maklad et al, 1979). The transplant volume increase in acute rejection was found, in a few cases, to precede the deterioration of the renal function as measured by plasma creatinine levels. The reversal of the rejection with treatment was associated with a return of volume to the previous level. Thus, the method can be used to diagnose early rejection and also reversal of changes as a result of effective therapy.

The transplant volume stabilised after the sixth month and correlated positively with the renal function of the transplant. We could not find a statistical difference between volumes of transplants treated with azathioprine and those treated with cyclosporin A, especially as the number of patients treated with cyclosporin A was small Further study will be needed to investigate the effects of cyclosporin A toxicity on transplant volume and whether transplant volume measurement could be a practical method for differentiating cyclosporin toxicity from acute or chronic rejection. Although in our study the diabetic patients were only five in number, they were found to have larger transplant volumes and better renal function than non-diabetics. This volume increase of about 25% compared with non-diabetics occurred in the first 6 months after the onset of diabetes following transplantation. Thus, diabetes affects the size and glomerular filtration rate of transplanted kidneys and normal kidneys in a similar way (Christiansen et al, 1982).

Finally, we found that renal transplant volume increased in pregnancy in the same way as in normal kidneys during pregnancy (Sims & Krantz, 1958; Lindheimer & Katz, 1977). This increase was not due to venous obstruction since the volume started to decrease well before delivery. At the same time it was noticed that pregnancy did not cause pelvic-ureteric dilatation in the transplant as it is reported to do in normal kidneys (Bailey & Rolleston, 1971).

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# Book review

*Pioneers and Early Years. A History of British Radiology.* By E. H. Burrows, pp viii+264, 1986 (Colophon Ltd, St Anne, Alderney), £32.50.
ISBN 0-9511676-0-X

Richard Mould's picture history of X rays and radium published a few years ago may have startled some radiologists who did not appreciate that such a new medical specialty could have a history However, the centenary of Röntgen's discovery will be in 1995, only eight years away. Dr Burrows is preparing us for this with the first major synopsis of British radiology since Pullin and Wiltshire's *X rays Past and Present* was written 60 years ago

Dr Burrows has amassed a vast amount of information in these pages The first four chapters deal with the discovery of X rays in Germany, the reception of the news in Britain, the first experimenters and the early apparatus and its makers The next three cover the founding and development of early X-ray departments in the London and provincial hospitals Radiological journals and societies, military radiology and radiation injury and its prevention are discussed in the last four chapters. The emphasis is on the development of radiodiagnosis, but Dr Burrows does not neglect the fact that the departments and all their staff dealt with therapy and diagnosis during the era under consideration The references are grouped between the text and the index, and, to the reviewer's delight, the sources of illustrations are documented in detail.

The chronological range of the book varies from chapter to chapter For example, "X rays on the Battlefield" describes only the first 5 years, plus a brief note on the teaching of radiography in the army, whereas radiological journals are covered up to 1930. This is justified, I believe, by the subject matter. Those researching in back volumes can be mystified by the frequent changes of title of the British radiological journals, which do not become recognisable to the modern radiologist until after the second world war Military radiology, on the other hand, becomes a much wider and more diffuse subject after 1914 and difficult to deal with in a general text

Integrating biographical material into thematic chapters poses problems which the author has dealt with in an unusual way. Each biographical entry is inserted in a smaller typeface in the chapter to which its subject relates. Where the subject's activities are treated in several chapters, the biography is split into two or more sections, which are cross-referenced The length of the biography varies from a couple of sentences to half a page or more The pioneers thus described are not only medical radiologists but also radiographers, physicists, physicians, manufacturers and electrical engineers As in the main text, these biographies include some material which will not be found in the radiological literature

The book is well produced, excellently printed and has well chosen illustrations, many of which have not been reproduced since their original publication. It is difficult to find misprints, and the few errors are minor ones The style is readable, the tale well told, and the reader is carried forwards by the momentum of discovery and development.

My only criticism is that, despite its title, the text is essentially a chronicle rather than a history No attempt is made to analyse the whys and wherefores, the forces and factors in the growth of this young medical specialty, with the exception of the chapter "Societies, Sections and the Institute" where the rival interests of the different professional groups are hinted at. There are some areas which are less thoroughly dealt with than others. For example, much more could have been written about early apparatus, but perhaps at the risk of disturbing the balance of the book

No doubt many books will be written on the history of radiology before the centenary There is now a small but growing body of historians and radiologists involved in research into radiological history. Several subjects have been scarcely touched: the development of barium studies, for example, or Dr Burrows' own specialty, neuroradiology Military radiology deserves a more intensive treatment than was possible in this volume. The technical background in photography, electrical engineering, vacuum science, glass making and metallurgy is an aspect which needs careful documentation before the demise of all the British craftsmen who once contributed to the X-ray industry Local studies of radiology departments in individual hospitals or geographical regions are becoming easier as the archives are rescued, catalogued and made accessible.

This volume deserves praise as a pioneer work, and should be bought and enjoyed by all who read this review.

Jean M. Guy

1987, *The British Journal of Radiology*, *60*, 531–533 JUNE 1987

# Prominent collateral vein in portal hypertension mimicking liver tumours: a pitfall in computed tomography

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(*Received July 1986 and in revised form October 1986*)

ABSTRACT

Computed tomography (CT) was performed on four patients with a prominent porto-systemic collateral vein, including three with an enlarged para-umbilical vein. We have observed a pitfall in non-contrast CT scans of patients with portal hypertension, in which a prominent collateral vein may mimic a liver tumour Dynamic CT as well as magnetic resonance imaging is of great value in such cases

Various porto-systemic collateral veins may develop in patients with portal hypertension. The ultrasonographic and computed tomographic features of this lesion have been described previously, yet the pitfall that a prominent collateral vein may be demonstrated as an intrahepatic mass lesion on computed tomography (CT) has not been described. The purpose of our report is to describe the appearance of a prominent collateral vein on CT and the role of dynamic CT in evaluation of this lesion.

## MATERIAL AND METHODS

Four patients with a prominent porto-systemic collateral vein were examined with CT using a dynamic scanning technique. There were two men and two women, aged 55 to 64 years. Angiographic confirmation was obtained in all cases. The entire liver was scanned, then a 60 ml bolus of Conray 400 (sodium iothalamate 67.5%, May & Baker Ltd) was injected intravenously. The area of interest was sequentially rescanned 20 s and 1–10 min after injection. A GE CT/T8800 whole-body scanner was used in most cases, with a scanning time of 9.6 s. The slice thickness was 10 mm, the slice interval 10–15 mm.

## CASE REPORTS

### *Case 1*

A 55-year-old woman was examined by CT for elucidation of idiopathic portal hypertension. A non-contrast CT scan showed a nodular, well defined mass with an identical CT density to that of the abdominal aorta, in the medial segment of the left lobe of the liver (Fig 1A). Cephalic scans at 15 mm and 30 mm showed similar hypodense masses in roughly the same coronal plane, and caudal scans showed small, oval, hypodense structures beneath the anterior abdominal wall. All masses enhanced in their entirety to the same degree as the portal trunk (Fig. 1B), and were isodense with the other abdominal vascular structures on delayed scans. A coeliac portogram proved that these masses were part of an enlarged para-umbilical vein (Fig. 1C).

### *Case 2*

A 64-year-old man with liver cirrhosis had a venous hum (Cruveilhier–Baumgarten murmur) in the epigastrium. A non-contrast CT scan showed a tubular, hypodense structure in the falciform ligament of the liver, which could be traced caudad beneath the anterior abdominal wall. A 15 mm cephalic scan showed another round, hypodense mass in the medial segment of the liver. Sequential scans following a bolus injection of contrast medium showed that these structures enhanced to the same degree as the portal trunk A superior mesenteric portogram clarified that they were part of an enlarged para-umbilical vein.

### *Case 3*

A 55-year-old woman with liver cirrhosis was referred for CT examination. A non-contrast CT scan showed tubular and round hypodense masses in the medial segment of the left lobe of the liver, and another smooth, round, almost equally hypodense mass in the posterior segment of the right lobe of the liver (Fig 2A) Subsequent scans following a bolus injection of contrast medium showed intense enhancement of the masses in the medial segment in their entirety, and confirmed the diagnosis of an enlarged para-umbilical vein. However, the mass in the posterior segment showed spreading, peripheral enhancement, on dynamic CT, characteristic of a cavernous haemangioma (Fig 2B). This patient was examined with a superconducting 1.5 T Magnetom (Siemens) A sagittal, spin-echo image with repetition time (TR) of 2.0 s and echo time (TE) of 35 ms showed the enlarged para-umbilical vein as multiple tubular low-intensity areas (Fig. 2C).

### *Case 4*

A 55-year-old man with liver cirrhosis was referred for CT examination. A non-contrast CT scan showed a hypodense, well defined mass in the medial segment of the left lobe of the liver After a bolus injection of contrast medium, the mass showed intense contrast enhancement, and a small draining vein behind the liver was delineated Superior mesenteric angiography and computed tomographic arteriography confirmed the diagnosis of a prominent porto-systemic shunt.

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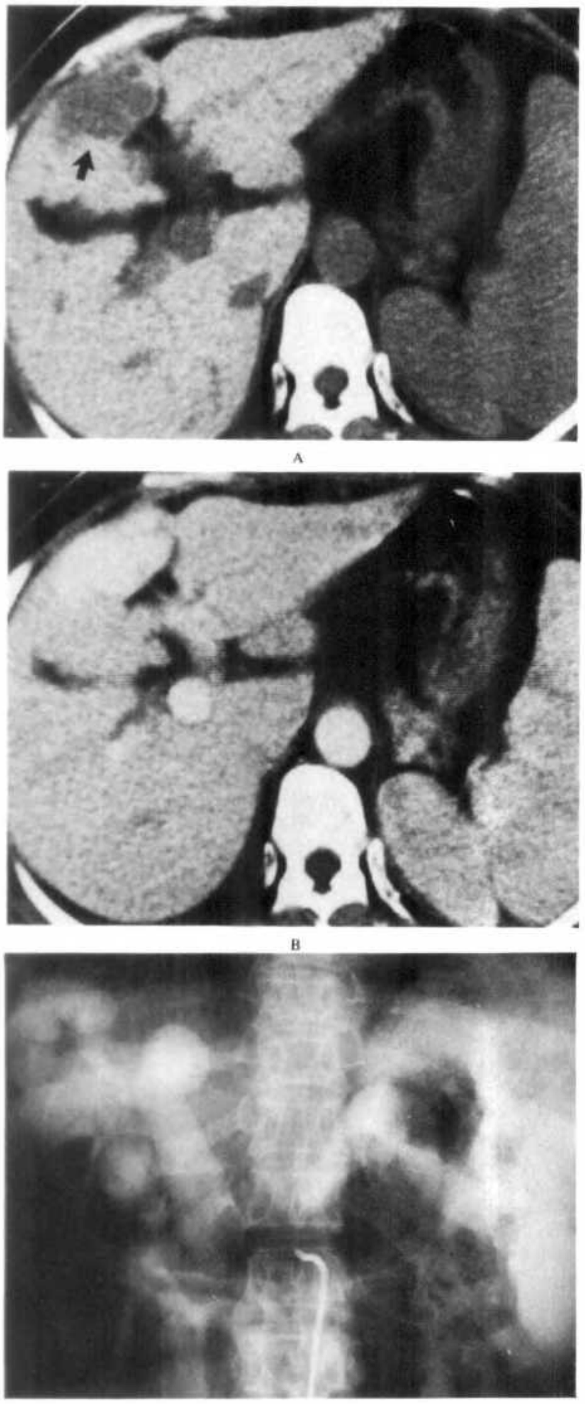
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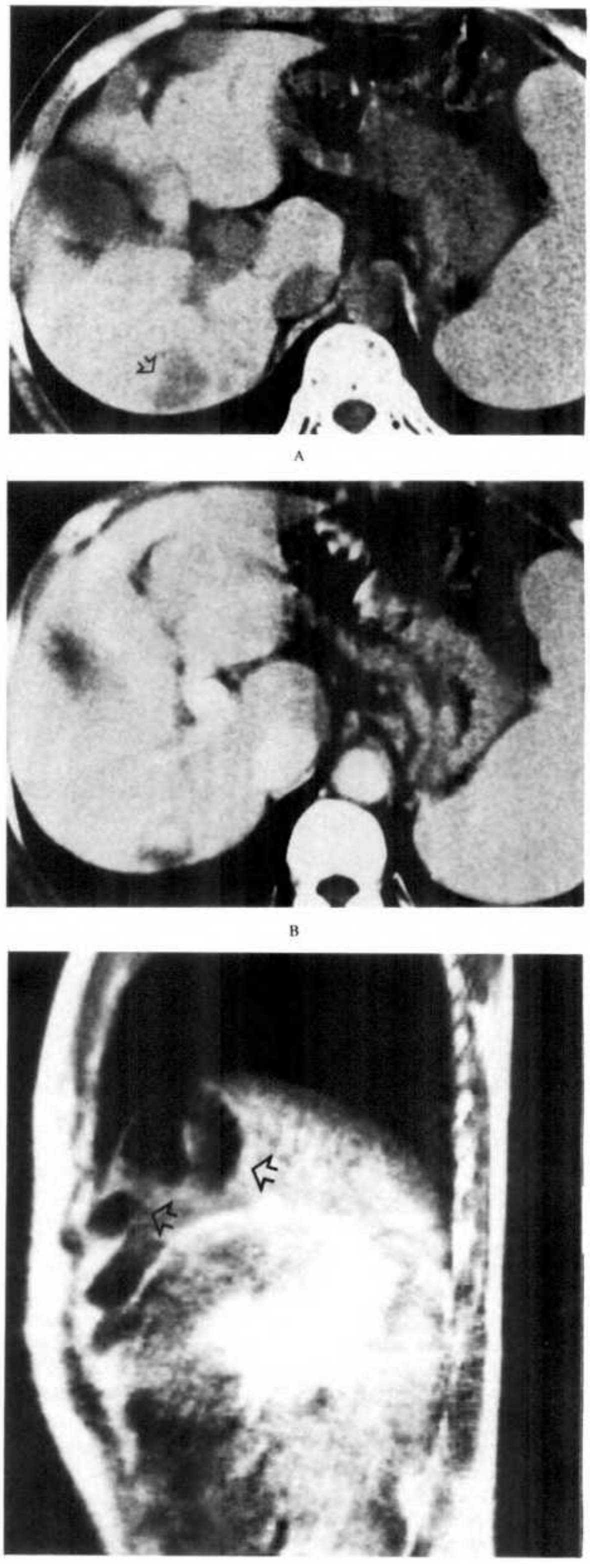
FIG. 1. *Case 1.*

(A) A non-contrast CT scan shows a hypodense mass in the medial segment of the left lobe of the liver (arrow). (B) A CT scan following a bolus injection of contrast medium shows that the mass undergoes intense enhancement in its entirety. (C) A coeliac portogram shows an enlarged para-umbilical vein.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## DISCUSSION

Ultrasonography is capable of demonstrating several types of porto-systemic collateral pathway including an enlarged para-umbilical vein, spleno-renal shunt or gastro-oesophageal varices (Juttner et al, 1982). The enlarged para-umbilical vein is visualised as a central sonolucent area in the echo-dense fat of the falciform ligament, which can be traced beneath the abdominal wall to the umbilical region. However, the diagnosis using ultrasonography may be difficult when a cirrhotic liver becomes so small that only a small part of the para-umbilical vein is demonstrated.

Computed tomography is an alternative method of demonstrating the abdominal collateral circulation in a non-invasive manner (Ishikawa et al, 1980; Park et al, 1981) and is especially indicated when ultrasonography is unable to exclude hepatocellular carcinoma in patients with liver cirrhosis. The para-umbilical vein originally has its course in the left sagittal fissure, but it may become enlarged and meandering in a patient with prominent portal hypertension. In such cases, the enlarged para-umbilical vein is demonstrated as a hypodense mass, usually located in the medial segment of the left lobe of the liver on CT, that may mimic a liver tumour in non-contrast scans. Similarly, other rare porto-systemic shunts may become prominent and mimic a liver tumour (Case 4). After a bolus injection of contrast medium, the porto-systemic collateral vein is enhanced in its entirety to the same degree as the portal trunk, while other liver tumours including hepatocellular carcinoma or cavernous haemangioma will show their characteristic contrast enhancement (Araki et al, 1980: Itai et al, 1980). Prominent porto-systemic collateral pathways are seen as multiple tubular structures containing little or no MR signal (Williams et al, 1985), an appearance which may aid the diagnosis (Case 3). Dynamic CT as well as MRI are of great value in differentiating prominent porto-systemic collateral veins and other liver lesions.

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FIG. 2. *Case 3.*

(A) Non-contrast CT scan showing tubular and round hypodense masses in the medial segment of the left lobe of the liver, and another round hypodense mass in the posterior segment of the right lobe of the liver (arrow). (B) Computed tomographic scans following a bolus injection of contrast medium confirm the diagnosis of enlarged para-umbilical vein and cavernous haemangioma in the posterior segment of the right lobe of the liver. (C) Sagittal spin-echo MR image with 2.0 s TR and 35 ms TE also confirms the diagnosis of enlarged para-umbilical vein (arrows).

# Book reviews

*Normal Variants and Pitfalls in Imaging*. Ed. by James B Vogler III, Clyde A. Helms and Peter W. Callen, pp. xvi+698, 1986 (W B Saunders Co., Philadelphia), £85 00
ISBN 0-7216-1457-4

Variations in normal radiological anatomy which may mimic disease have received appropriate recognition in the radiological literature over the years. The classic works of Koehler and Keats, for instance, are standard references on these variants. The complexity of modern imaging, besides giving a further perception of anatomical variants, causes artefacts which demand the awareness of the diagnostic radiologist

This large volume describes anatomical variants and artefacts in computed tomography (CT), ultrasound, nuclear medicine, magnetic resonance imaging, mammography and digital subtraction angiography. Some pathological conditions are included in order to give a direct comparison with the variants and other pitfalls which may mimic them and, secondly, to demonstrate how artefacts may obscure disease The sections on the various modalities are divided into chapters based on anatomical systems. Running heads direct the reader to specific anatomical sites, although a comprehensive index also aids the user

The illustrations are generally of a very high quality and well laid out, being enhanced by lucid captions and a generous use of indicators. The largest section is on CT and it is this which would probably be the most useful in practice, although some of the paediatric CT scans are not of optimal quality A minor criticism in the ultrasound section is the use of both positive and negative modes, sometimes in the same case

A work of this scope is obviously an enormous undertaking. While the range of items must be sufficiently comprehensive to produce a useful reference book, the personal choice of the compiler sets the standard. The difficulties are compounded in this particular book by the rapid developments in these modern imaging modalities, bringing with them further diagnostic traps for the unwary. This ambitious book succeeds in being a very helpful practical guide in a loosely defined area It can be recommended as a bench book in any well equipped imaging department Trainees would be well advised to read the pertinent section before commencing any of these modalities

G H. WHITEHOUSE

*Notes on Radiological Emergencies*, 3rd edit. By George Ansell, pp. 15, 1986 (Blackwell Scientific Publications, Oxford), £6.50.
ISBN 0-632-01729-5

The third edition of this well known publication brings up-to-date, expert advice on the treatment of emergencies which may occur during radiological procedures

The major part of this booklet is, of course, devoted to adverse reactions to radiological contrast media The technical and drug advice (doses, routes of administration, incompatibilities, etc.) can hardly be bettered, although I think the use of a salbutamol inhaler for bronchospasm should be included. There is no discussion of low-osmolar contrast media and their advantages, particularly for high-risk patients. That issue is of major and growing importance for all practising radiologists, who are rightly concerned about the increased cost (by a factor of five) of the newer, safer products I hope the next edition will at least mention this problem.

This reviewer regards this clearly presented, flip-over, multicoloured stiff card publication so highly that he advises that every practising radiologist, radiographer and nurse working in the department of radiology should be familiar with its contents and prepare their emergency trolley accordingly The maroon hard cover of this booklet should be a well displayed, immediately available feature in every department of radiology There is no way by which we can forecast when a severe reaction may occur The best advice and preparation is to follow the succinct instructions in this booklet. Thank you, George Ansell

R. G. GRAINGER

1987, *The British Journal of Radiology*, *60*, 535–541 JUNE 1987

# Delineation of the spleen by a combination of proliposomes with water-soluble contrast media: an experimental study using computed tomography

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*(Received June 1986 and in revised form December 1986)*

ABSTRACT

Numerous methods for delineating the splenic pulp, including dynamic computed tomography scanning, either are unreliable or have other shortcomings. A method is described for enhancing the spleen using aqueous contrast media in conjunction with proliposomes. While liposomal carrier systems have previously been used for diagnostic purposes, proliposomes circumvent many of the problems associated with the manufacture and handling of liposomes. This enhancement is based on the selective uptake of particulate material by the reticuloendothelial system. While others, by using washed liposomal suspensions, have apparently obtained higher degrees of splenic contrast enhancement, the present study nevertheless shows that significant levels of enhancement are obtainable by a combination of intra- and extraliposomal contrast media.

In patients with lymphoma, especially Hodgkin's disease, the ability to detect splenic involvement by non-invasive means would be very important in patient management. The spleen is involved by lymphoma in one third of cases at the time of presentation (Castellino, 1983). Furthermore, one third of patients with Hodgkin's disease and splenomegaly have no histological evidence of lymphoma in the spleen, while one third of spleens in Hodgkin's and non-Hodgkin's lymphoma are normal in size but do contain lymphoma (Kaplan et al, 1973). As splenic involvement is often the only focus of abdominal disease found at laparotomy, the ability to detect lymphomatous infiltration of the spleen with accuracy might obviate the need for staging laparotomy in many patients (Harell et al, 1977).

Computed tomography (CT), enhanced by intravenous water-soluble contrast medium, is inaccurate in assessing lymphomatous involvement of the spleen (Redman et al, 1977; Jones et al, 1978; Glazer et al, 1981; Zornoza & Ginaldi, 1981). Attempts have been made to target the reticuloendothelial system of the liver and spleen with particulate contrast media (Vermess et al, 1979, 1982). While effective in delineating small liver metastases (Lewis et al, 1982) and lymphomatous infiltration within the spleen (Thomas et al, 1982), agents such as emulsified poppy seed oil have a high incidence of side-effects (Lamarque et al, 1979; Miller et al, 1984).

A further method of delineating the liver and spleen on CT has been the use of liposomes (Havron et al, 1981). These are phospholipid vesicles with the ability to entrap a wide range of material including drugs and contrast media. It was the uptake of liposomes by cells of the reticuloendothelial system, especially the spleen (Sharma et al, 1977), that suggested the incorporation of contrast media into liposomes for hepatosplenic CT. One of the fundamental constraints of liposome utilisation has been their commercial production. The reasons for this are numerous but include the problems of large-scale manufacture of a sterile product with defined and reproducible properties, displaying adequate chemical and physical stability. Conventional aqueous liposome suspensions may be subject to a variety of detrimental effects. Some liposome formulations may aggregate or fuse on storage and their component phospholipids may undergo hydrolysis (Frøkjaer et al, 1984). Careful choice of formulation may alleviate some of these problems, although toxicological considerations may preclude their use in certain instances.

The proliposome concept (Payne et al, 1985, 1986a) has been developed to circumvent many of the potential problems associated with aqueous liposome dispersions. Proliposomes are a dry, free-flowing granular product composed of a water-soluble carrier material, such as sorbitol, coated with dry liposomal components, for instance phospholipids plus sterol. The addition of water to proliposomes, above the phase transition temperature of the component phospholipid(s), results in the formation of an isotonic liposomal suspension. The size of liposomes derived from proliposomes may be modified by careful choice of formulation; for example, inclusion of increasing amounts of negatively charged phospholipid can markedly decrease liposome size (Payne et al, 1986a). Studies have indicated that the size profiles of liposomes derived from proliposomes are consistent and relatively unaffected by either proliposome particle size or hydration temperature (Payne et al, 1986b). Ideal candidates for inclusion in proliposomes are lipophilic compounds which partition preferentially into the liposomal lipid phase upon proliposome hydration. Nevertheless, as will be shown in this study, it is possible to utilise water-soluble compounds in conjunction with proliposomes

While large-scale batches of proliposomes can readily be made under sterile conditions, the small-scale batches used in this study were not made aseptically. However, it was anticipated that the nature of the process, involving large quantities of methanol together with pyrogen-free sorbitol, would result in a sterile product. The material used in this study was subsequently found to be sterile.

## MATERIALS AND METHODS

### *Materials*

Egg lecithin was obtained from Honeywill and Stein Ltd (Wallington, Surrey). Cholesterol was obtained from Sigma Chemical Company (Poole, Dorset). Renografin 76 (370 mg I/ml) and iopamidol (370 mg I/ml) were both obtained from the Squibb Institute for Medical Research (Princeton, New Jersey, USA) Both solutions were diluted with water for injection to give 148 mg I/ml. Sorbitol (pyrogen-free) was obtained from Roquette UK (Tunbridge Wells, Kent). All other materials used were of Analytical Reagent grade

### *Methods*

*Preparation of placebo proliposomes.* The liposome formulation utilised in these studies was similar to one described by Ryan et al (1983) and was chosen to maximise entrapment of contrast agent.

In a typical batch, egg lecithin (3.90 g) and cholesterol (0.94 g) were dissolved in chloroform (75 ml) to give a phospholipid–sterol molar ratio of 7.3. Aliquots of solution (5–10 ml) were then deposited sequentially *in vacuo* on to 20 g sorbitol (125–500 $\mu$m size cut) according to the method detailed by Payne et al (1985) A weight ratio of sorbitol to liposomal components of 4.13:1 was utilised throughout. The resultant material was then sieved to remove material less than 75 $\mu$m and greater than 600 $\mu$m in diameter Portions of proliposomal material (0.621 g) were stored under nitrogen (less than 1% oxygen) in clear glass vials at $-20$°C.

*Hydration of proliposomes.* Placebo proliposomes (0.621 g) were hydrated with 1.5 ml Renografin (15% v/v) at 20–25°C. The volume and concentration of Renografin was chosen to maximise the degree of entrapment while ensuring liposome formation. Transmission electron microscopy, using the procedure described by Payne et al (1986a), showed the liposome suspension to contain principally multilamellar structures.

*Determination of liposome entrapment efficiency.* The entrapment efficiency of liposomes containing either Renografin or iopamidol was determined by estimating the proportion of contrast medium entrapped in liposomes. Non-encapsulated contrast medium was first removed by gel filtration (Fry et al, 1978) Liposome integrity was destroyed by the addition of 50% v/v aqueous methanol and the concentration of contrast medium was determined spectrophotometrically. The entrapment efficiency was a consistent feature for each formulation type. Lipid concentration was determined by the method of Stewart (1980) Since phospholipid and cholesterol were an intimate "mixture" in the formulation, assay of one component, the phospholipid, was sufficient to determine entrapment efficiency The phospholipid concentration of the liposome suspension was calculated as 80.7 mg/ml.

*Liposome particle size analysis.* Particle-size analysis of liposome suspensions was performed on a Coulter TA II multichannel particle sizer using a 50 $\mu$m-orifice tube.

### *Animal model*

Groups of three Sprague–Dawley rats (300–400 g) were each anaesthetised with 0·1 ml Immobilon (Reckitt & Colman) intramuscularly Each group of rats was then injected via the femoral vein with up to 0.75 ml contrast medium, so that each group received one formulation/dose level only. Two dose levels, 120 mg I/kg and 240 mg I/kg, were utilised in this study. The rate of injection was kept constant throughout at 1.5 ml/min.

### *Computed tomography*

A General Electric CT9800 scanner was used for these studies. Transverse sections, 1.5 mm thick, were taken at 10 mm intervals through the upper abdomen. A 512 × 512 matrix was employed with a field of view of 18 cm or 20 cm and a scan time of 2 s.

The attenuation values (HU) within the liver, spleen and renal parenchyma were found using regions of interest at corresponding points at each stage of the experiments The region of interest in each case was four pixels. The pixel size varied between 0.35 mm$^2$ and 0.39 mm$^2$ because of differences in the field of view used. This analysis gave a region of interest which varied in size between 0.49 mm$^2$ ((0.35 mm)$^2 \times 4$) and 0.61 mm$^2$ ((0.39 mm)$^2 \times 4$), although the size was consistent in each experiment Readings were taken pre-contrast and 10, 20, 30, 45 and 60 min after injection of contrast agents. Longer experimental times were not practicable due to the heavy clinical workload of the scanner unit.

## RESULTS

Particle-size analysis of Renografin and iopamidol liposomes indicated mass median volume-equivalent diameters of 2.95 $\mu$m (SD $\pm$ 1.93 $\mu$m) and 4.40 $\mu$m (SD $\pm$ 1.53 $\mu$m) respectively. Since the proliposomes used with each of the contrast agents were of the same formulation, liposome size differences may be the result of differences in contrast-agent electrical charge.

Liposome size differences were also reflected in contrast-agent encapsulation efficiencies. Thus, about 28% of the Renografin present was liposome-encapsulated whilst about 38% of iopamidol was

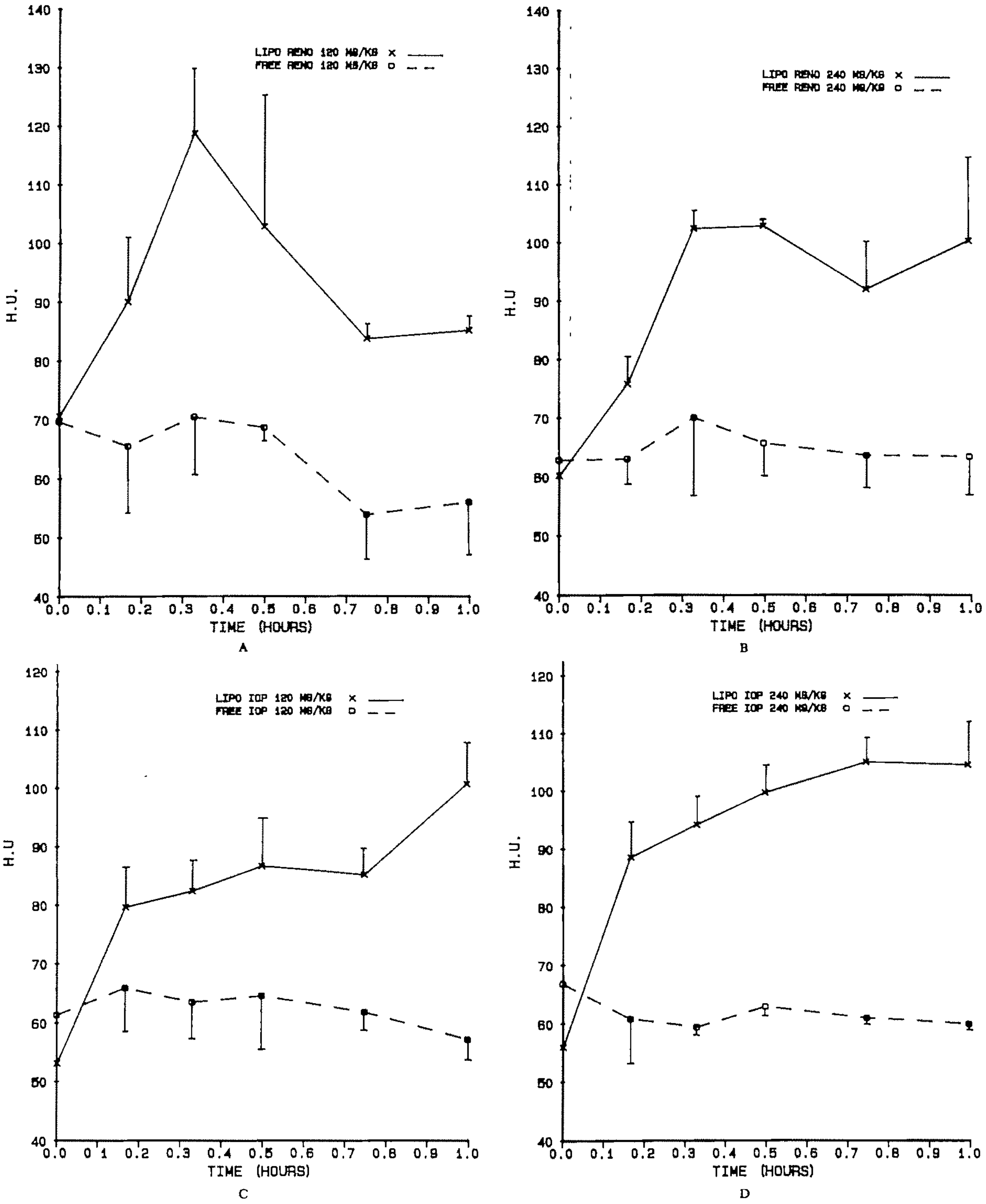


FIG 1

Spleen Comparison of enhancement by free and liposome-entrapped contrast media. variation of attenuation (±SD) with time (A) Renografin 120 mg I/kg, (B) Renografin 240 mg I/kg, (C) iopamidol 120 mg I/kg, (D) iopamidol 240 mg I/kg Solid line represents liposome-entrapped contrast media and broken line represents free contrast media in this and all subsequent figures entrapped. Extraliposomal contrast agent, therefore, constituted the majority of the injected dose. Consequently, elimination kinetics of contrast agent probably involved both free and encapsulated forms of the material. No attempt has been made to quantify leakage of contrast medium from the liposomes following injection.

Maximum enhancement of the spleen, with liposomes containing either Renografin or iopamidol at doses of 120 mg I/kg and 240 mg I/kg body weight was reached between 15 min and 30 min after injection (Fig 1). The average ($n = 3$) increase in attenuation per mg of iodine per kg body weight was respectively 0.38 and 0.18 HU/mg I/kg for liposomal Renografin at 120 mg I/kg and 240 mg I/kg. In contrast, free Renografin gave no contrast enhancement at these doses. With regard to liposomal iopamidol, average ($n = 3$) increases in attenuation of 0.38 HU and 0.21 HU/mg I/kg were obtained at doses of respectively 120 mg I/kg and 240 mg I/kg Unencapsulated iopamidol gave no increase in contrast enhancement at either dose

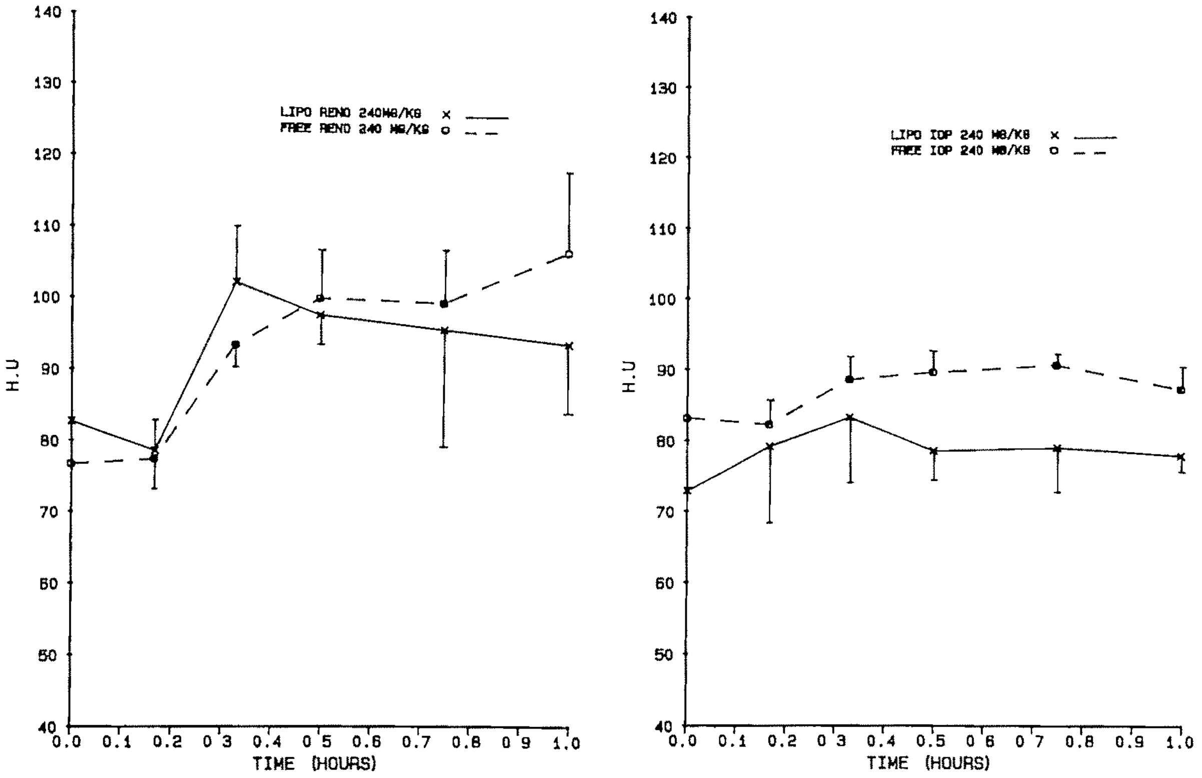
Differences in contrast enhancement between liposomal and free Renografin or iopamidol were much less pronounced in the case of the liver (Fig. 2).

In general, excretion of liposomal contrast media by the kidneys was delayed in comparison with non-encapsulated contrast media (Fig. 3). Typical homogeneous enhancement effect of liposomal contrast agent on rat spleen is shown in Fig. 4.

## DISCUSSION

In an effort to target contrast medium more specifically to organs of interest, various carrier vehicles have been proposed These include red blood cell ghosts, plastic beads, aggregated albumin and liposomes (Gregoriadis, 1976). The use of liposomes as a delivery system has been exploited by many workers, either as a carrier for water-soluble contrast media (Havron et al, 1981; Ryan et al, 1983,1984; Seltzer et al, 1984) or, alternatively, as a targeted contrast agent *per se* (Caride et al, 1982).

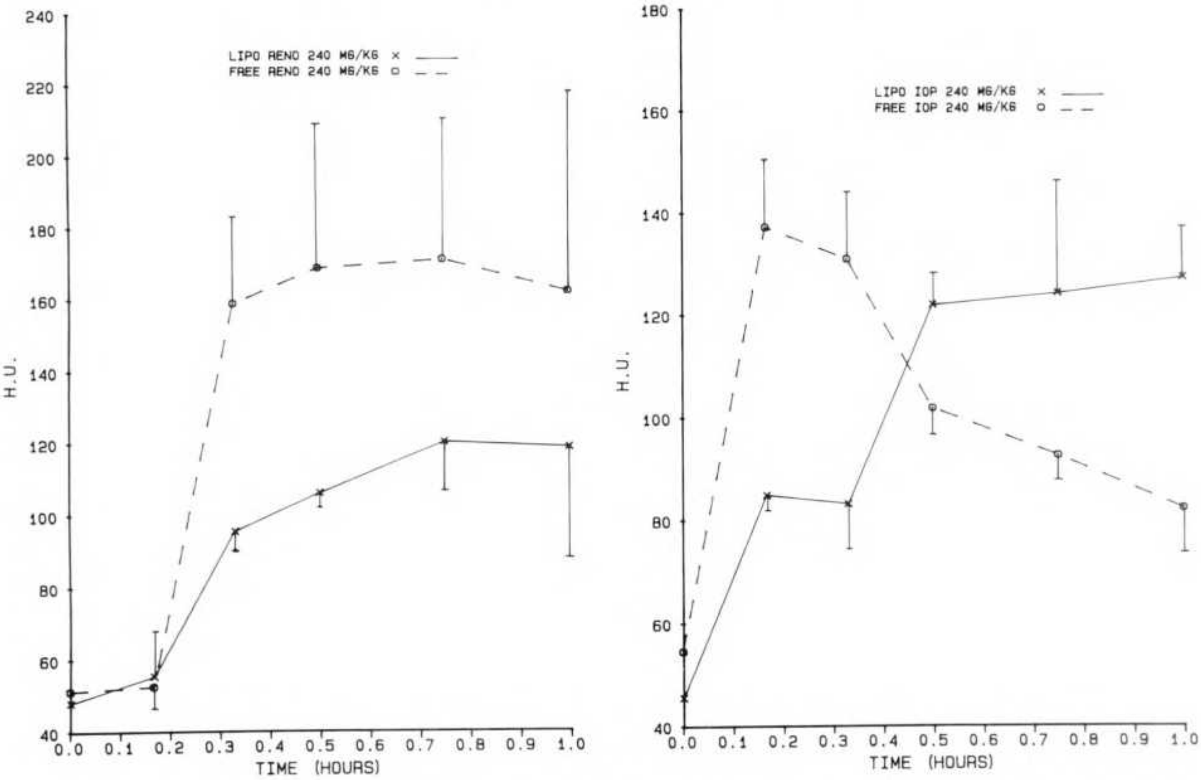
Havron et al (1981) encapsulated 76% sodium methylglucamine diatrizoate (Renografin 76) in liposomes and administered them intravenously to rats and rabbits. Spleen and liver attenuation values were highest 30–60 min after injection and gradually declined over 24 h, with a mean increase in attenuation of 2.9 HU and 0.4 HU per mg of iodine respectively for the spleen and



A B

FIG. 2

Liver. Comparison of enhancement (±SD) by free and liposomal contrast media and time (A) Renografin 240 mg I/kg, (B) iopamidol 240 mg I/kg.

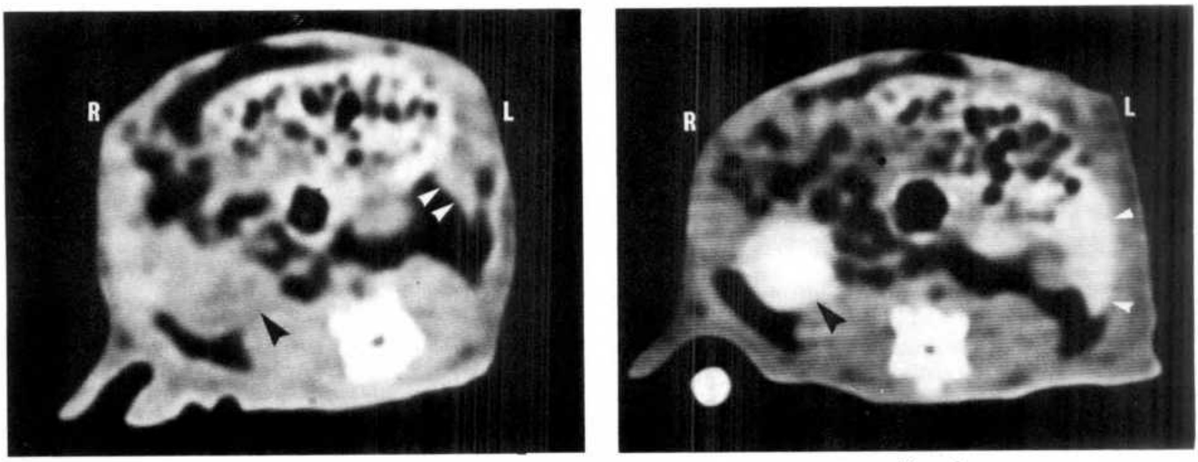


A

B

FIG. 3.

Kidney. Comparison of enhancement (±SD) by free and liposomal contrast media and time. (A) Renografin 240 mg I/kg, (B) iopamidol 240 mg I/kg.



A

B

FIG. 4.

A CT scan of a rat abdomen (A) before contrast-medium injection and (B) 30 min after injection of liposomal iopamidol 240 mg I/kg. There is opacification of the spleen (white arrow heads) and the kidney (black arrow heads).

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liver of rats at a dose of 4 mg I/kg. Splenic enhancement, at 5 HU/mg I, was even higher in rabbits. Substantial renal excretion was noted by Havron et al, as in the present series. Rozenberg et al (1984), also using water-soluble contrast media in liposomes, claimed to detect neoplastic or inflammatory lesions as small as 1 mm in mice and 10 mm in dogs using conventional radiography. Iosefamate, a hepatobiliary contrast medium, has also been encapsulated in liposomes and has opacified the liver and spleen of dogs (Seltzer et al, 1984).

Ryan et al (1983), to improve further the limiting factor of water-soluble contrast-media entrapment, introduced the non-ionic contrast agent metrizamide into liposomes The lower molarity of metrizamide resulted in a twofold increase in entrapment compared with diatrizoate. Attenuation in the rat spleen was increased by 200 HU with metrizamide, compared with an increase of 130 HU using diatrizoate. In both instances, Ryan et al (1983) found maximum values 1 h after injection. Using diatrizoate encapsulated by liposomes, splenic attenuation in the rat increased by 2 27 HU/mg I/kg body weight results which are very similar to those of Havron et al (1981). Hepatic enhancement followed a similar course, a rapid rise during 15 min being followed by a slower rise over the next 45 min, although the increase in enhancement was only 0.25 HU/mg I/kg body weight.

Most workers in the field have employed washed liposomal suspensions, that is, freed from non-encapsulated contrast agent. While this approach has clear advantages, the feasibility of obtaining washed liposomal suspensions of defined and reproducible characteristics may well have limitations in clinical practice Instead, we have opted to utilise a system in which both free and encapsulated contrast medium are present, non-encapsulated contrast medium being removed by gel filtration when determining entrapment efficiency. A consistent product can thus be ensured and no complex manipulations are required during preparation. Phospholipids of low phase transition temperature, about −15°C, have been chosen to ensure true liposome formation at room temperature The long-term stability of placebo proliposomes hydrated with water-soluble contrast medium was not determined, since the product was used immediately after preparation In the dry state, proliposomes are stable for at least 2 years. Since doses of 120 mg/kg or 240 mg/kg of free Renografin or iopamidol failed to elicit significant contrast enhancement, it is reasonable to suppose that non-encapsulated contrast agent in the liposomal preparations behaved similarly. It is therefore likely that the contrast enhancement of the spleen, for a particular dose of iodine, would have been higher if all of the injected contrast medium was encapsulated by liposomes than in the present preparation, where approximately two thirds of the contrast medium was in a free form. The presence of this additional non-encapsulated contrast medium may well account for the discrepancy between these results and those of Havron et al (1981) and Ryan et al (1984). The observation by Zherbin et al (1982), that a species-specific, low hepatic–splenic enhancement ratio occurs in rodents may explain the low contrast enhancement of the liver.

Acknowledgment

We are grateful to Peter Noble for his help in this study

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# Book reviews

*Diagnostic Procedures in Pancreatic Disease.* Ed. by P Malfertheiner and H Ditschuneit, pp xiii+331, 1986 (Springer-Verlag, Berlin), DM128.
ISBN 3-540-16395-6 (Berlin)
0-387-16395-6 (New York)

This compact, glossy-paged book represents the proceedings of a symposium held in Ulm, West Germany, in March 1985 The title suggests yet another recitation of the pancreatic investigative repertoire but, in fact, the text also includes a rich mixture of clinical observation, physiology, pathophysiology and pathology. The editors are to be congratulated on their choice of contributors, who range from acknowledged pioneers with didactic styles to today's leading researchers, whose refreshing and forthright approach mounts a much-needed challenge to "dogma" with regard to the aetiogenesis of pancreatitis.

The text is arranged conventionally: definitions, acute pancreatitis, with pathomorphology followed by imaging methods, physiology, biochemistry, and tests of pancreatic dysfunction to assist diagnosis or facilitate prognosis; chronic pancreatitis, which is presented in similar format; and pancreatic cancer, incorporating recent work using monoclonal antibodies I do not know any other book on the pancreas, of similar size, in which so much new information is carefully presented. Every trainee radiologist should have access to a copy, while those intending to pursue a career in gastrointestinal radiology should invest in one, despite the cost, because the chapters on imaging methods are likely to stand the test of time, at least for the foreseeable future. There are top-quality reproductions of ultrasound scans (including those produced by the endoscopic route), pancreatograms (both endoscopic and percutaneous), and contrast-enhanced computed tomography (CT) scans Furthermore, each imaging modality is placed in proper perspective with attention to predictive value, applicability and cost effectiveness· contrast-enhanced CT emerges as a powerful index of pancreatic necrosis at an early stage in acute pancreatitis. Consultant gastroenterologists and researchers in every discipline in pancreatology will learn a great deal from this little gem of a book—as I have

J. M. BRAGANZA

*High-resolution Computed Tomography of the Paranasal Sinuses, Pharynx and Related Regions.* By Gertrude Maatman, pp ix+171, 1986 (Martinus Nijhoff Publishers, Dordrecht), £41.86.
ISBN 0-89838-802-3

Reading this book, one is struck by the tremendous enthusiasm the author has for her subject and the amount of care with which it has been written. It has a short opening chapter on the author's technique for scanning the sinuses and pharynx, followed by two extensive chapters, the first on general anatomy, the second on computed tomographic anatomy; together they comprise nearly half the book. These chapters are very detailed and contain many clearly labelled illustrative axial and coronal scans. The author stresses the need to recognise detailed normal anatomy in order to assess pathological changes accurately and she describes the lymphatic drainage and common routes of spread of tumours at various sites. My only criticism of this section is that the illustrations are sometimes divorced from the accompanying text and there are occasional spelling and typing errors.

The remaining two chapters discuss the pathology of the sinuses, and pharynx and oral cavity respectively. Each starts with a brief review of the literature, which is then followed by a retrospective analysis of the diagnostic and therapeutic impact of computed tomography in the author's own practice.

Numerous illustrative cases complete each chapter but unfortunately these are grouped under their diagnostic/therapeutic scores rather than pathology, for ease of reference, which I think was a mistake. The cases reviewed obviously reflect the author's practice and the majority are of malignant tumours. There is only one trauma case and this important topic is therefore barely touched upon

This is a very individual book which is probably too specialised for most radiology department libraries, but anyone closely involved with ear, nose and throat scanning, whether radiologist, surgeon or radiotherapist, should find its excellent anatomy section extremely valuable.

F E. WHITE

1987, *The British Journal of Radiology*, 60, 543–546 JUNE 1987

# The "shrunken" pancreas: a morphological variant of idiopathic chronic pancreatitis

By *Oscar Bulgim, D.Med.y Cir., Adrian Manning, M.D., M.R.C.P. (U.K.), David Lintott, M.B., B.S., F.R.C.R. and Anthony Axon, M.D., F.R.C.P.

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(*Received July 1986 and in revised form September 1986*)

ABSTRACT

Six patients with idiopathic chronic pancreatitis are described in whom a pancreatogram showed an unusual morphology, being irregularly narrowed throughout. This "shrunken" appearance differs from the classic irregular dilatation usually seen in chronic pancreatitis. Two of the patients had inflammatory bowel disease, none had a history of alcoholism and only one had gallstones.

Endoscopic retrograde cholangiopancreatography (ERCP) has become a standard technique for the investigation of patients with known or suspected pancreatic disease (Vennes & Silvis, 1983; Axon & Mitchell, 1984). Changes seen in chronic pancreatitis are variable, but typically there is dilatation and irregularity of the main pancreatic duct and, although there may be stenoses and obstruction, the overall width of the duct is greater than normal. Similarly, side-branches may demonstrate nipping at their origins with dilatation beyond, an irregular branching pattern and often shortening (Rohrmann et al, 1974; Freeny & Lawson, 1982). Occasionally, however, patients with chronic pancreatitis demonstrate diffuse and irregular narrowing of the main duct and side-branches, sometimes but not always with shortening, giving an overall "shrunken" appearance. This appearance is unusual and we describe in this paper six such patients and suggest that they may represent a subgroup of pancreatitis which is probably idiopathic, although it may be associated with inflammatory bowel disease.

Over a period of 11 years ERCP was performed in 3529 cases. In 362 patients the changes associated with chronic pancreatitis were seen and, of these, six were found to have a pancreas with a "shrunken" appearance. In each case the duct system was considered to be adequately filled although injection of contrast medium often required a greater pressure than usual.

## CASE REPORTS

*Case 1*

A 60-year-old man was admitted for investigation of hepatosplenomegaly and ascites and was found to have portal hypertension Two years later he developed jaundice and a liver biopsy revealed periportal fibrosis. This was attributed to arsenic exposure as, on examination, he was found to have Bowen's disease; he was involved in handling pig food which contained arsenic. There was no history of alcohol abuse The portal vein was calcified but patent on angiography and gross varices were present At ERCP the pancreatogram showed diffuse irregular narrowing and overall reduction in size of the gland (Fig. 1). Gallstones were present in the common bile duct, which showed extrinsic compression in the region of the portal-vein calcification Pancreatic calcification and cysts were seen on computed tomography (CT) and a Lundh test was normal During laparotomy for a distal splenorenal shunt the pancreas was noted to be small and fibrotic

*Case 2*

A 56-year-old man presented with a 4-week history suggestive of steatorrhoea and weight loss of 1 stone He had had acute pancreatitis the previous year, but did not abuse alcohol Further investigation revealed a stone-free, non-dilated biliary tree, but at ERCP there was a narrowed pancreatic duct with a fine, beaded contour (Fig. 2). The main duct was normal in length but the side-branches were generally shortened although probably normal in number A Lundh test was abnormal with a mean tryptic activity (MTA) of 6 7 IU/ml. A subsequent rectal biopsy showed idiopathic inflammatory bowel disease.

*Case 3*

A 34-year-old man presented with a 1-year history of malaise and right upper quadrant abdominal pain Over the previous 6 months the pain had been radiating to the left hypochondrium and back and he had developed steatorrhoea and lost 1 stone in weight. He had not abused alcohol Endoscopic retrograde cholangiopancreatography demonstrated a narrowed main pancreatic duct which was irregular throughout with few demonstrable side-branches (Fig. 3) Faecal fat was 139 (normal 18) mmol/24 h. A Lundh test gave a MTA of 0 7 IU/ml; the pancreas was seen to be small on CT and no gallstones were detected on ultrasound.

*Case 4*

A 16-year-old man with a 10-week history of intermittent epigastric pain radiating into both hypochondria had developed diarrhoea with blood and mucus and became jaundiced. The jaundice was settling at the time of his admission, but liver function tests suggested cholestasis with a normal serum amylase level. On ERCP gross irregular narrowing throughout the pancreatic duct was evident, with tapering and bowing of the intrapancreatic common bile duct (Fig 4). A Lundh test was abnormal with a MTA of 2 IU/ml.

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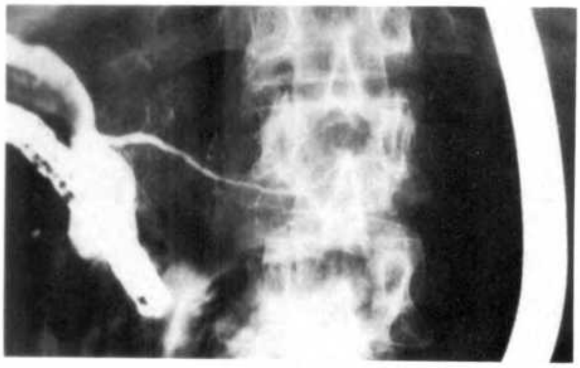

FIG. 1. *Case 1.*
The duct system shows diffuse irregular narrowing with an overall reduction in size of the pancreas.

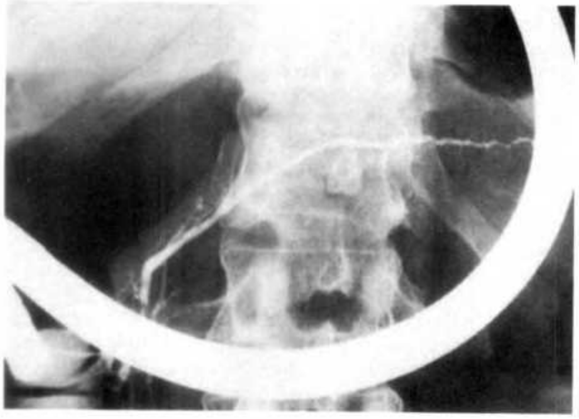

FIG. 2. *Case 2.*
The main duct is narrow and irregular. It is normal in length but the side-branches are shortened in all regions.

Further investigation showed severe total ulcerative colitis which required colectomy. At laparotomy the body of the pancreas was seen to be thickened and inflamed.

*Case 5*

A 45-year-old woman sought medical advice because of a 1-week history of epigastric pain radiating to both hypochondria and to the back and the shoulder. This was followed by jaundice. She did not abuse alcohol. Serum enzyme analysis demonstrated cholestasis; she had a normal abdominal ultrasound scan and CT scan, but ERCP showed irregular narrowing of the main pancreatic duct and side-branches but without any shortening (Fig. 5). There was also an intrapancreatic common-bile-duct stricture without proximal dilatation. Faecal fat was 83 mmol/24 h and a Lundh test gave MTA as 0.7 IU/ml.

*Case 6*

A 31-year-old man was referred with an 8-month history of backache, steatorrhoea and weight loss. He did not abuse alcohol. Previous investigations had revealed elevated serum amylase levels during episodes of pain. An abdominal ultrasound scan was within normal limits and ERCP showed a small and irregularly narrowed pancreatogram and normal cholangiogram (Fig. 6).

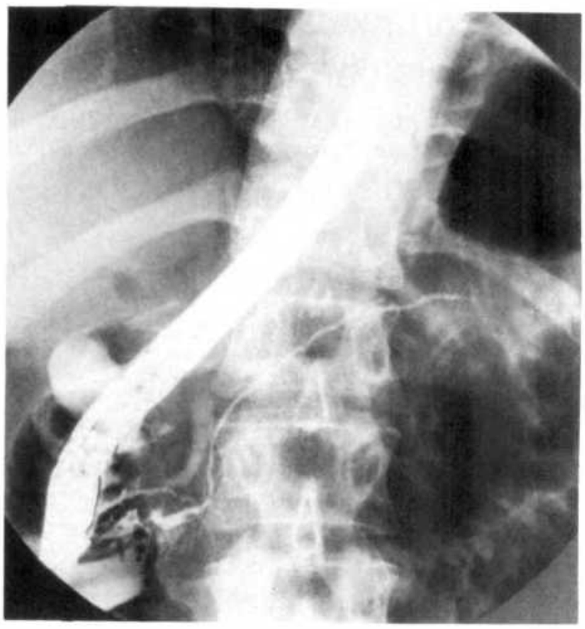

FIG. 3. *Case 3.*
The main duct is markedly narrowed along the whole of its length with the exception of a short segment immediately adjacent to the ampulla. Only a few side-branches in the head are visible.

## DISCUSSION

The pancreatogram in each of these six patients showed diffuse irregular narrowing throughout the duct system. While this appearance was most obvious in the main pancreatic duct as 16.2 ± 2.5 cm. However, this is the side-branches in four of the six examples. In no case was there any abnormal duct dilatation as is typically seen in chronic pancreatitis. Despite this, the appearances can be classified as severe diffuse chronic pancreatitis according to the criteria of the Cambridge classification (Axon et al, 1984).

Kasugai et al (1972) defined the normal length of the main pancreatic duct as 16.2 ± 2.5 cm. However, this is often difficult to measure accurately because of foreshortening resulting from normal variations in position and shape of the gland. Assessments of pancreatic size are therefore somewhat subjective. Three of these cases had pancreatograms which definitely appeared shortened, while the other three were of normal length. The assessment of duct length depends of course on complete contrast opacification. In all of these cases the pancreatogram was considered to be as complete as possible, although in several the injection of contrast medium required a considerably greater pressure than is usually required for pancreatography.

There is clear evidence of pancreatic disease in these patients using criteria other than ERCP and, with the

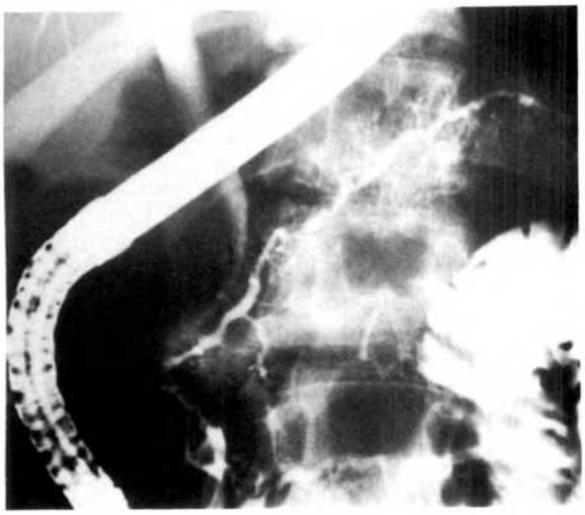

FIG. 4. *Case 4.*

There are marked calibre irregularities along the length of the main duct without abnormal dilatation at any point. Coarse parenchymal opacification largely obscures side-branch detail, but the overall appearance is one of diffuse irregular narrowing. Note also tapering and bowing of the intrapancreatic common bile duct.

possible exception of Case 4 which could have represented an episode of acute pancreatitis, there is independent evidence that each had chronic pancreatitis. In Case 1 the pancreas was seen to be atrophic at surgery; in Case 2 there was an abnormal Lundh test with clinical steatorrhoea; in Case 3 there was an abnormal Lundh test, steatorrhoea and abnormal CT; Case 4 had an abnormal Lundh test; Case 5 had an abnormal Lundh test and gross steatorrhoea; and Case 6 had clinical steatorrhoea.

No histology is available to indicate a cause for the narrowed ducts. It is unlikely that these patients had acute on chronic pancreatitis with oedema of the gland leading to temporary narrowing of the main duct, as we have not seen these appearances in other patients known to have acute pancreatitis. Nor have we seen them in patients with chronic pancreatitis of known aetiology. It is likely, therefore, that they do represent a genuine subgroup of chronic pancreatitis. Apart from Case 1, where gallstones were present, no disorder regarded as a potential cause of pancreatic disease was found: there was no evidence of alcoholism (Sarles, 1974); no patients had received drugs known to cause pancreatitis (Mallory & Kern, 1980); none had a family history of the disorder (Grand et al, 1983); serum calcium level was normal (Mixter et al, 1962); none had developmental anomalies of the pancreatic duct or duodenum which could have predisposed to the condition (Worning, 1984). One patient had been exposed to arsenic, but this association has not been reported previously and it is not likely that arsenic was the cause of his pancreatitis. Two patients had proven inflammatory bowel disease, neither having sclerosing cholangitis. There have been several reports of an association between inflammatory bowel disease and

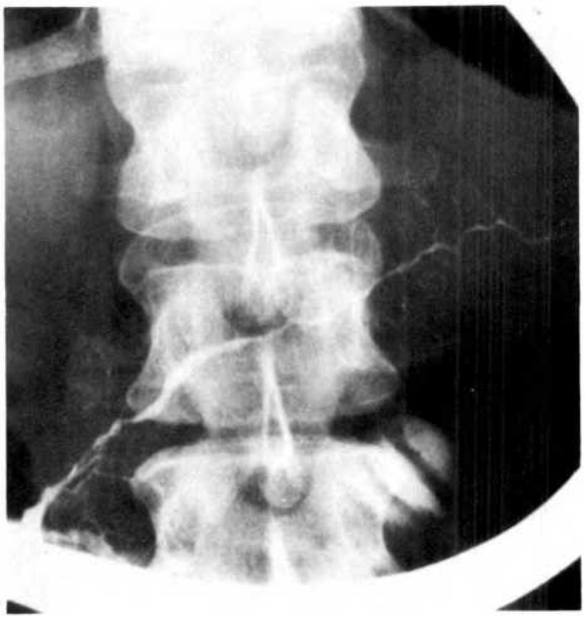

FIG. 5. *Case 5.*

Diffuse irregular narrowing of the main duct and side-branches throughout the gland without any overall shortening.

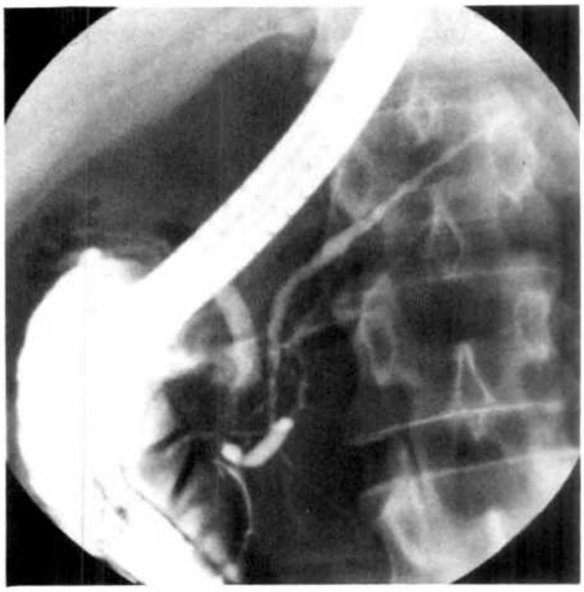

FIG. 6. *Case 6.*

The main duct is irregularly narrowed and probably also shortened. Despite good cannulation and firm injection, no further duct opacification occurred.

pancreatic disease (Warren & Sommers, 1949; Ball et al, 1950; Axon et al, 1979; Gurian & Keeffe, 1982; Borkje et al, 1985; Seyrig et al, 1985) and Case 4 had been reported previously in this context (Axon et al, 1979). Pancreatic manifestations may antedate symptoms of inflammatory bowel disease and the bowel disease may not be severe, suggesting that pancreatic disease is not secondary to the inflammatory bowel disease but simply an association. This raises the possibility that there might be some common aetiological or predisposing factor.

ACKNOWLEDGMENT

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# Inadvertent inflation of the balloon: a rare but serious complication of Miller-Abbott intubation

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(*Received August 1986*)

ABSTRACT

Inadvertent injection of contrast medium or tube feedings into the wrong port of a Miller–Abbott tube can be catastrophic. Four cases are reported, three of which required emergency surgery and two resulted in small-bowel infarction. This complication can easily be avoided if the attending physician and radiologist are aware of the entity.

The Miller–Abbott (MA) tube is a double-lumen radio-opaque rubber tube, commonly used for gastrointestinal intubation in suspected small-bowel obstruction. One lumen provides access for suction or feeding, and the second lumen provides access for the injection of mercury into a balloon at the tip of the tube. The mercury-weighted balloon allows the peristaltic activity of gastrointestinal tract to carry the MA tube distally. A Y-shaped adapter with both lumens labelled is provided by the manufacturer.

Inadvertent injection of tube feedings, contrast media or medications will distend the balloon with potentially disastrous results. An extensive search of the literature revealed only three reports (Walker, 1940; Hafner et al, 1961; Wyatt & Chisholm, 1984) of such a complication. We report four patients with MA tube complications encountered during the past 3 years.

## CASE REPORTS

### *Case 1*

A 60-year-old man was admitted with an 8-week history of a 40 pound weight loss. Intravenous urography revealed bilateral hydronephrosis due to distal ureteric obstruction. Cystoscopy and biopsy revealed a primary carcinoma of the bladder. The patient underwent a radical cystectomy, bilateral pelvic node dissection, and formation of an ileal conduit.

Post-operatively, the patient developed a prolonged adynamic ileus which was treated with MA intubation. When symptoms persisted, approximately 300 cm$^3$ of Renografin were injected through the MA tube to investigate the possibility of a small-bowel obstruction. What was interpreted as a dilated segment of jejunum was noted radiographically (Fig. 1). An abdominal radiograph 2 h later showed no change in this "opacified segment of small intestine". The patient's intestinal complaints intensified, and he was re-explored for a small-bowel obstruction.

At surgery, a necrotic segment of small bowel was discovered, resulting from the contrast medium-distended MA tube balloon. An entero-enterostomy was performed and the patient recovered uneventfully.

### *Case 2*

A 25-year-old man underwent exploratory laparotomy with lysis of adhesions and small-intestinal resection for obstruction. Two weeks after a stormy post-operative course, the patient was recovering and placed on tube feedings through an MA tube which had been placed at the time of surgery. Following one of his feedings, the patient developed nausea and vomiting which persisted despite nasogastric suction. The next day an abdominal radiograph revealed linear gas densities parallel to the wall of the proximal jejunum (Fig. 2). Bowel

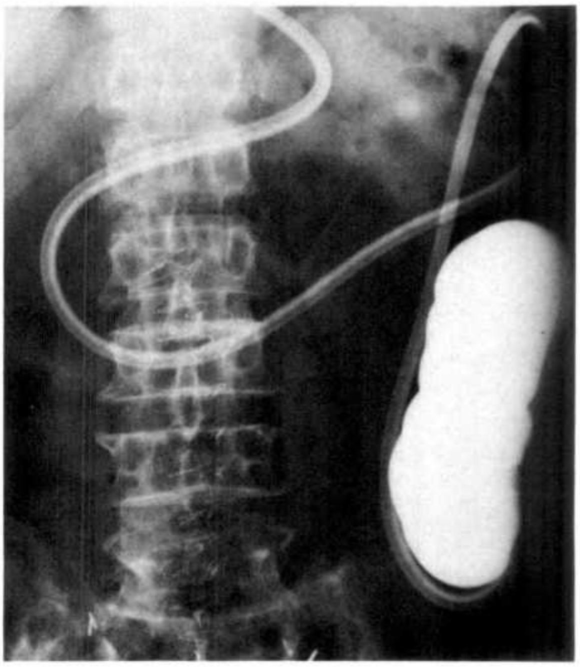

FIG. 1.

Abdominal radiograph (AP) shows the MA tube coiled in the proximal jejunum. The balloon is filled with 30% Renografin and mimics an opacified loop of jejunum. Note the lack of valvulae conniventes in the opacified "loop".

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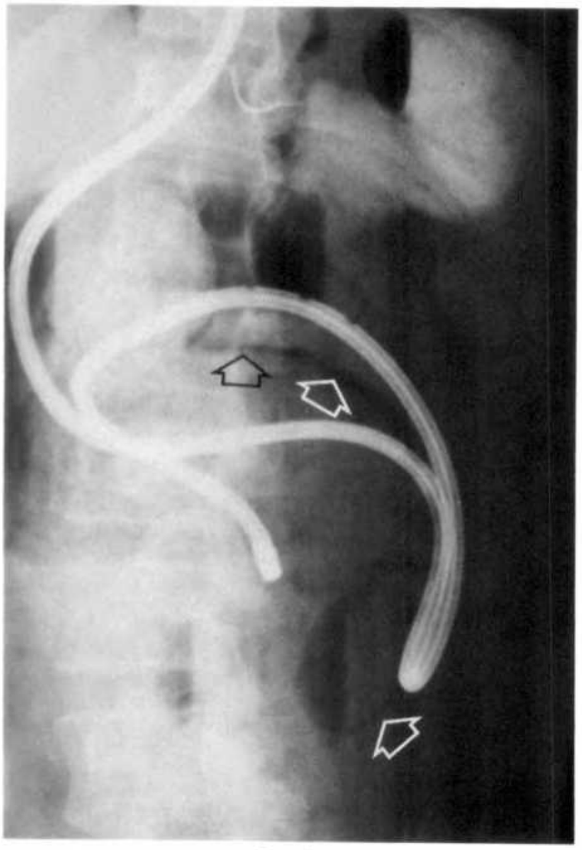

FIG. 2.

Abdominal radiograph (left lateral decubitus view) shows the MA tube coiled in the proximal jejunum. Curvilinear air densities can be seen along the bowel wall (arrows).

infarction was suspected and the patient was re-explored. At surgery a single loop of necrotic proximal jejunum was discovered, distended by an inflated balloon. Approximately 350 cm$^3$ of Osmolite (liquid feed; Abbott Laboratories) were aspirated. The necrotic bowel was resected and an entero-enterostomy was performed. The patient recovered uneventfully.

*Case 3*

A 57-year-old woman was admitted with a 5-day history of nausea, vomiting and gripping abdominal pain. The patient had had an appendectomy approximately 20 years previously. The symptoms persisted despite rehydration and nasogastric decompression, and the patient underwent exploratory laparotomy on the second hospital day. Obstructing

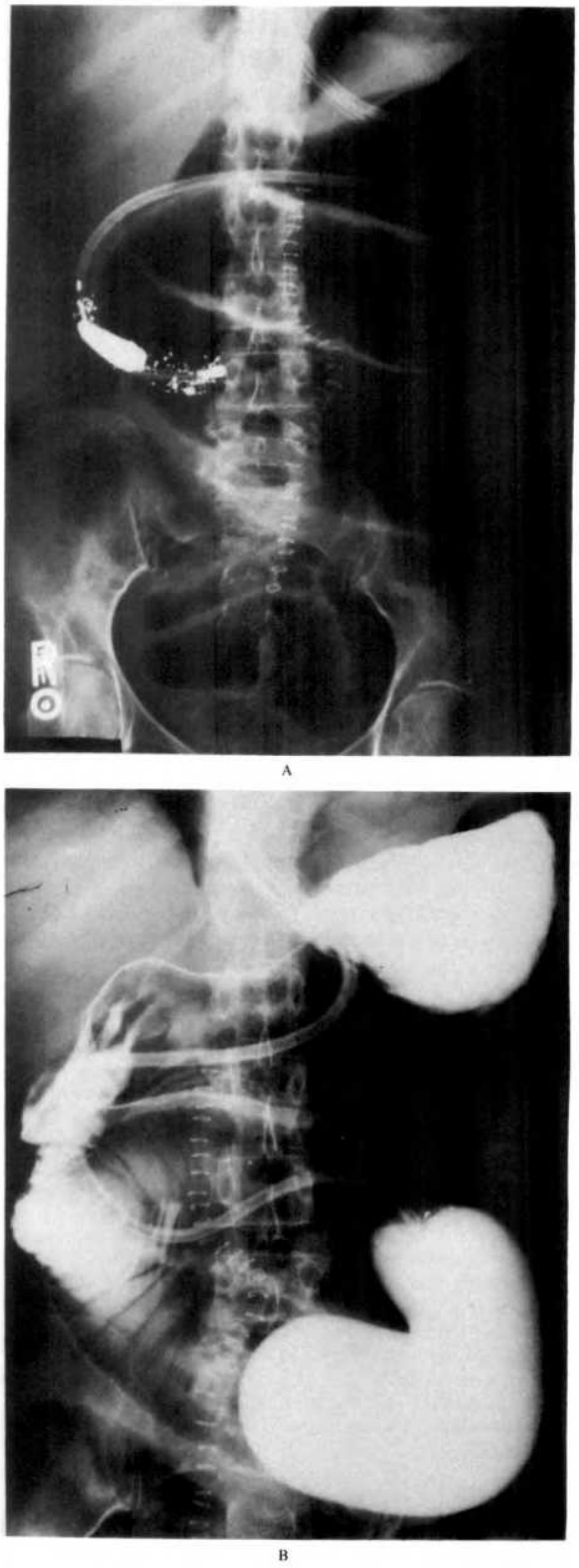

FIG. 3.

(A) Abdominal radiograph (AP) shows dilated jejunal loops in the mid-abdomen and left upper quadrant. The tip of the MA tube is in the third part of the duodenum. (B) Abdominal radiograph (AP) shows the smooth contour of the opacified balloon as opposed to valvulae conniventes in the opacified jejunal loops.

adhesive bands were divided and the patient did well until the fifth day when she developed a recurrence of symtoms. An MA tube was inserted for intestinal decompression (Fig. 3A). The patient was rescheduled for a second exploratory laparotomy following the development of fever and leucocytosis. A contrast examination was obtained prior to surgery to localise the site of obstruction.

Under fluoroscopy, a mixture of thin barium was injected through the MA tube, opacifying a "proximal segment of jejunum". This barium did not progress distally and additional barium could not be injected because of increasing resistance. The patient was given oral barium which opacified the stomach and proximal jejunal loops (Fig. 3B).

The patient was taken immediately to surgery where multiple small-bowel adhesions were divided. The MA tube balloon was filled with barium but was not obstructing the bowel. The balloon was deflated by aspiration and the patient recovered uneventfully.

*Case 4*

A 90-year-old woman was found to have a Stage 2B cervical carcinoma 5 months prior to this admission. She had received a full course of radiation therapy and 3 days prior to admission she developed increasing nausea and vomiting. Physical examination and abdominal radiographs indicated a small-intestinal obstruction, and the patient underwent exploratory laparotomy with division of adhesions in the proximal and mid-ileum. A Miller–Abbott tube was placed intraoperatively to the level of the distal jejunum for decompression. The patient was started on tube feedings on the seventh post-operative day. On the 10th day the patient developed abdominal distension, nausea and vomiting. A barium examination was performed and the small bowel was found to be obstructed at the level of the balloon of the MA tube, which was distended (Fig. 4). Approximately 150 cm$^3$ of clear fluid were aspirated from the balloon, relieving the obstruction. The patient recovered uneventfully and was discharged 1 week later.

## DISCUSSION

The MA tube is commonly used both pre- and post-operatively for the following purposes: (1) to decompress an obstructed small bowel, (2) to provide access for contrast injection to diagnose the presence, the site or the cause of small-bowel obstruction, (3) to serve as an intraoperative guide to the site of an obstruction, (4) to reduce post-surgical complications and (5) to administer tube feedings, electrolytes, or medication. Smith (1945) has shown that the pre-operative use of an MA tube reduces surgical morbidity and mortality.

Complications with the use of the MA tube have been emphasised (Cantor, 1949; Ingelfinger, 1978; Ghahremani, 1981). The most common complications are related to fluid and electrolyte disturbances caused by long-term gastrointestinal suction. Less common complications are related to the mechanical presence of the tube. The complications can be divided into minor and major types.

Minor complications (Chaffee, 1949; Cohen & Silverstein, 1952; Hafner et al, 1961; Hunter et al, 1981) including epistaxis, nasal obstruction (nose plug), sinusitis, eustachian salpingitis, pharyngitis, acute otitis media, laryngeal oedema and abscess of the nasal septum have all been reported. These complications are due to mechanical excoriation of the nasopharyngeal mucosa and are more frequently seen in children. Other minor complications reported are inadvertent tracheal intubation, aspiration pneumonia and spillage of mercury into the gastrointestinal tract or tracheobronchial tree.

Major complications (Chaffee, 1949; Lichtenstein, 1952; Hafner et al, 1961; Sower & Wratten, 1965; Fricke & Niewodowski, 1976; Bredfeldt & Moeller, 1978; Ghahremani, 1981; Hunter et al, 1981; Redmond et al, 1982; Wyatt & Chisholm, 1984): a variety of severe complications have been reported. These include laryngeal obstruction, gastric or intestinal perforation, haemorrhage from ruptured oesophageal varices, oesophageal stricture, antegrade or retrograde intussusception, systemic mercury intoxication, gaseous distension of the balloon, and a knotted or coiled tube being impossible to withdraw. Many of these complications require surgical intervention and some of them have even been fatal.

Injecting tube feedings, medicine or even contrast medium into the wrong port will inflate the balloon and may cause intestinal obstruction. If the obstruction is

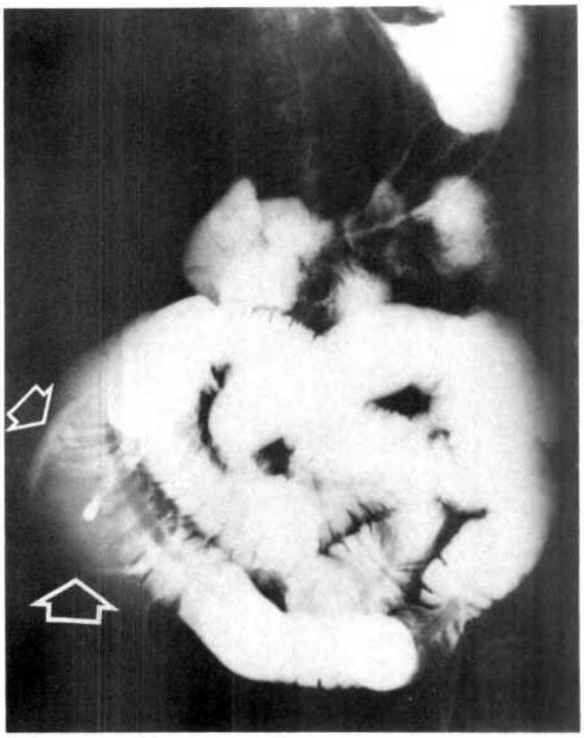

FIG. 4.

Barium small-bowel study shows the distended balloon (arrows) of the MA tube causing intestinal obstruction at the level of the distal jejunum.

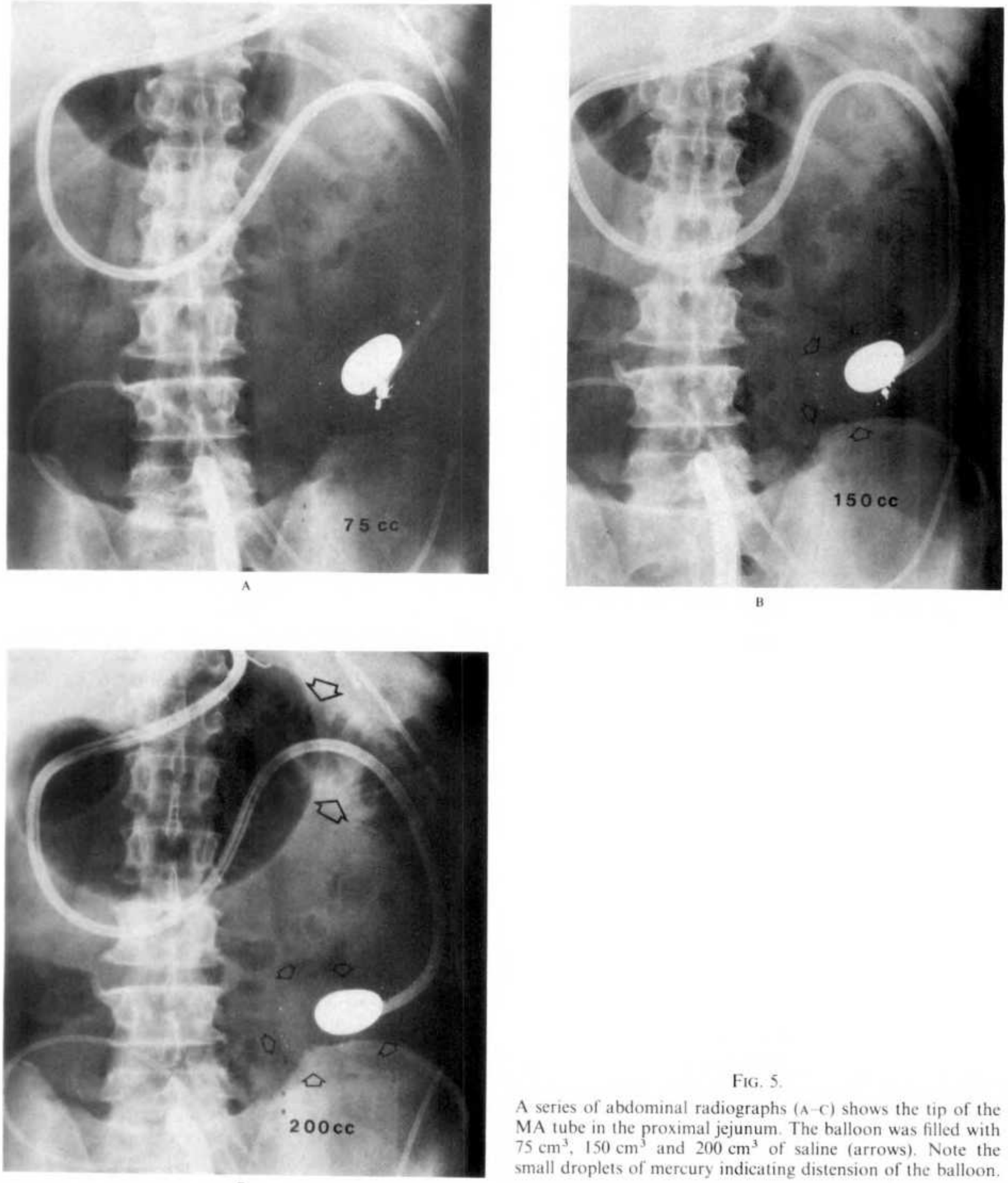

FIG. 5.

A series of abdominal radiographs (A–C) shows the tip of the MA tube in the proximal jejunum. The balloon was filled with 75 cm$^3$, 150 cm$^3$ and 200 cm$^3$ of saline (arrows). Note the small droplets of mercury indicating distension of the balloon.

not recognised immediately, bowel infarction or even death can result. Although the MA tube is commonly used, an extensive literature search revealed only three reports of such a complication. Walker (1940) reported difficulty in withdrawing an MA tube with an inflated balloon filled with feeding material, the lumen leading to the balloon having become plugged with the feeding material. After repeatedly forcefully pulling the balloon against the cardia of stomach, the balloon burst and the tube was withdrawn without complication

Hafner et al (1961) reported that nurses frequently injected medications through the wrong lumen, accounting for difficulties in extubation. One of Hafner's cases required increased inflation of air to burst the balloon to allow withdrawal.

Wyatt and Chisholm (1984) reported a fatal complication. A 9-year-old boy recovering post-operatively from a ruptured appendix developed intestinal obstruction secondary to a distended balloon filled with feeding material. When the balloon could not be deflated, surgery revealed a gangrenous loop of terminal ileum The patient had a stormy post-operative course and died 48 h later.

Our cases, as well as those already published, reveal that injection of liquid agents into the wrong port of the MA tube do occur and may have serious sequelae. The radiographic diagnosis of a balloon distended with non-opaque material can be difficult. The only findings may be an oval or tubular mass of soft-tissue density. The presence of unusual air collections near the tip of an MA tube may also be helpful. Numerous tiny mercury droplets scattered throughout an oval mass of soft-tissue density (Fig. 5A–C) is strong evidence of an over-distended balloon.

While the injection of contrast material into the MA tube balloon would seem to be a simple radiographic diagnosis, this complication was not recognised fluoroscopically in two of our cases (Cases 1 and 3) due to a lack of familiarity with the mechanics of the MA tube. Immediate recognition would have obviated the need for further surgery. Awareness of the potential complications and the lack of valvulae conniventes seen in an opacified "loop" which does not change in size and shape radiographically should immediately raise the possibility of filling of the balloon.

None of our patients experienced abdominal pain during the balloon inflation. This was probably due to their overall physical condition and the already dilated loops of small bowel, allowing the balloon to reach a significantly large size

We estimated how much fluid could be injected into the balloon before a patient would experience pain by sequential injections of saline in a volunteer patient who was being treated for Ogilvie's syndrome with both a rectal and an MA tube (Fig. 5A–C). Only when 200 cm$^3$ of normal saline were introduced into the balloon did the patient experience mild epigastric discomfort. Immediate aspiration of the saline was followed by cessation of the patient's discomfort. This patient was alert, and the response to balloon inflation was very minimal but patients who are seriously ill or who already have abdominal symptoms may demonstrate little response to an inflated balloon.

We performed an *in-vitro* study and found that Osmolite or a standard barium mixture can be slowly aspirated from the balloon through a 20 gauge needle. If the lumen of the MA tube has been occluded with injected material, it may be possible to aspirate a dilated balloon percutaneously or to rupture the balloon endoscopically. In certain circumstances this may be a more acceptable method of treatment than surgical re-exploration.

We have reported four cases of what is ordinarily an uncommon complication of the use of the MA tube. The attending physicians and radiologist must be familiar with the purpose of the double-lumen construction of the MA tube if serious or potentially fatal complications are to be avoided.

ACKNOWLEDGMENT

The authors wish to thank Ms Sharron Shackelford for her secretarial assistance

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# Book reviews

*Clark's Positioning in Radiography,* 11th edit. Ed. by R. A. Swallow, E. Naylor, E. J. Roebuck and A. S. Whitley, pp. 418, 1986 (William Heinemann Medical Books, London), £45.00. ISBN 0–433–18838–3

This revised edition of *Clark's Positioning in Radiography* has updated this standard reference of radiographic technique. The editors, R A. Swallow and E. Naylor, and assistant editors, E. J Roebuck and A. S. Whitley, have reorganised the book so that all plain radiographic techniques are now included. The new-format Introduction discusses the basic principles of radiography and considers image quality in terms of contrast, sharpness, magnification and distortion and guidance is given on the choice of exposure factors. The necessity for radiation protection is emphasised and there is a list of rules and recommendations in line with current regulations. Radiographic terminology is carefully explained; in fact the whole Introduction, with the aid of diagrams, photographs and radiographs, presents information that is concise and easily assimilated.

Subsequent sections commence with a list of recommended projections for each area of the body, followed by illustrations of positioning and resultant radiographs. In this volume the relevant text is adjacent to each illustration, making it much simpler to follow than hitherto On the whole, the quality of the illustrations is good and it is refreshing to see the new positioning photographs, although many of the "old familiar faces" still appear. Examples of various pathological conditions and common positioning errors are included, but this section could have been further improved by the inclusion of evaluation criteria used to judge the technical acceptability of various projections.

An improvement over the 10th edition is the grouping together of all aspects of skull and dental radiography in one volume. It is interesting to see the new dental formula and description of both parallel bisecting-angle techniques for intraoral radiography. Three new sections have been introduced· Ward Radiography, Theatre Radiography and Skeletal System Survey These provide general information covering equipment, aspects of patient care and hospital practice, as well as the practical aspects of positioning. The Skeletal System Survey provides a chart giving easy reference to choice of projections required for diagnosis of various bone conditions and demonstrates radiographic examples of some of these. Although this section concentrates on plain radiography, it is emphasised that other methods,. particularly radionuclide imaging, are of great value when making a diagnosis.

This book has succeeded in presenting the essentials of radiographic technique in a logical sequence and in as practical a form as possible. It provides easy reference to the most widely used and up-to-date radiographic techniques, presenting the information in a clear and concise manner It is a must for every department, especially those with radiology and radiography students I look forward to the companion volume on contrast media and special imaging techniques.

BRENDA LOVELAND

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*Practice of Coronary Angioplasty.* By T. Ischinger, pp. 325, 1986 (Springer-Verlag, Berlin), DM198.
ISBN 3–540–15949–5 (Berlin)
0–387–15949–5 (New York)

This book is an excellent collection of chapters dealing with coronary angioplasty and has covered most of the important issues. A particularly useful chapter was the one on clinical selection and the role of non-invasive testing before percutaneous transluminal coronary angioplasty (PTCA) It compared the major chronic stable angina trials of CASS, VA and ECSS studies in a logical manner without overstating the case for performing PTCA

When discussing the indications and contraindications for PTCA personal bias is evident as there are no adequate double-blind trials to prove some of the conclusions: not all people accept the dogma that the purpose of both coronary bypass surgery and PTCA is complete myocardial revascularisation Partial revascularisation may produce excellent clinical results as well.

There is no mention of the very important question of emergency surgery in the catheter laboratory. There should be some input by the anaesthetists and surgeons in the planning of the catheter laboratory.

Angioplasty equipment is not dealt with completely, but this is such a changing field that the authors have accepted that the chapter deals with the instruments they use and that some of the information would be outdated at the time of publication. Very few people are using the older systems and there is little merit in describing them.

The objections to some statements are minor. On balance this is an excellent book and worth owning and using as a reference and guide to this important subject.

P. GISHEN

1987, *The British Journal of Radiology*, *60*, 553–556 June 1987

# Out-of-hours radiology: a suitable case for audit?

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## Abstract

An outline of radiological activity outside normal working hours over a 2-month period in a teaching hospital is presented. A 100-fold variation between specialties in the number of requests per 100 discharges and deaths is shown. Specialties with a high out-of-hours radiology demand also tended to have a high overall demand. Chest and abdomen radiographs accounted for approximately 82% of all investigations undertaken during the period of observation. Six radiological investigations—chest and abdomen radiographs, computed tomography, skull radiographs, intravenous urography and cardiac catheterisation—accounted for approximately 94% of all out-of-hours investigations. There was a 5.6-fold variation between investigations in the time taken to carry out one standard unit of work. In the health authority studied, it was estimated that £93 000 was spent on radiographers' out-of-hours payments in 1984/85, of which almost 90% was directly related to the number of radiological procedures undertaken It is suggested that the wide variation in rates of out-of-hours radiology usage between specialties requires more detailed examination. The limited range of procedures accounting for the great majority of the out-of-hours work makes a study feasible. The very marked variation in the time taken for one unit of work may result in important financial distortions if clinical budgeting becomes more widespread. The large excess cost of out-of-hours radiological investigations, which may be as much as £16 000 000 per annum in England and Wales, offers the possibility of substantial savings if some of the investigations are shown to be of little clinical value outside normal working hours.

For several decades, there has been a steady rise in radiographic workload in developed countries. For instance, the number of radiographic units of work in England has recently been increasing at a rate of 5–10% per annum (Bull, 1974; Abrams, 1979; Sherwood, 1979; Wrighton & Oliver, 1980) implying a doubling of workload every 7 to 14 years. This has outstripped the growth in the number of consultant radiologists and radiographers, which has been about 3% and 4% per annum, respectively (Wrighton & Oliver, 1980).

The increase in demand cannot be attributed to a disproportionate increase in complex investigations There has been only a modest fall in the proportion of simpler examinations and a slight rise in complex examinations (Abrams, 1979). The proportion of radiographic workload generated by general practitioners and accident and emergency departments did not increase significantly in the decade 1968–77 (Abrams, 1979). The only marked change has been a tendency for a greater proportion of the work to arise from inpatient rather than outpatient referrals. Since the increase in demand has not been matched by an increase in resources, consideration has had to be given to mechanisms for reducing demand. This requires that the process is more fully understood than at present.

There is evidence that radiology and pathology tests sometimes fail to contribute to clinical decisions about diagnosis and management (Carmalt & Whitehead, 1971; Bull, 1974; Sandler, 1979). Usage in different hospitals for patients with the same diagnosis has been shown to vary by factors of between four and 24 (Ashley, 1974) and there is a twofold variation in the number of inpatient radiographic work units per 1000 discharges and deaths between regions in England (Rees et al, 1976).

Radiological investigations outside normal working hours have received little attention in the literature. The higher unit cost of out-of-hours radiology investigations makes it important that this aspect of diagnostic radiology usage should be described and costed as a first step to understanding the reasons for the requests and their clinical usefulness, in order to decide whether resources could be put to better use. If studies demonstrate that many of these investigations contribute little to decisions on patient management, it might be possible to limit out-of-hours requests without compromising the quality of care. It is also possible that even if many radiographs cannot be avoided, performing them inside rather than outside normal working hours might be found to be clinically acceptable. A guideline has been reported to have reduced by half the out-of-hours use of chemical pathology tests (Lester, 1985). The present paper describes the use of out-of-hours radiological investigations over a 2-month period in a teaching hospital.

## Materials and Methods

In the teaching hospital studied, radiographers submit claims for payments for out-of-hours work, as set out in current terms of service (Department of Health and Social Security (DHSS), 1981). Using these forms, the following data were collected for August and September 1984: the radiographer's name, the place from which the call was undertaken, the patient's name and ward, the name of the requesting doctor, the work undertaken (radiographs, searching for films, splicing

TABLE I

Out-of-hours radiology usage by specialty

| Specialty | Requests per 100 deaths & discharges | % of units used out of hours |
|---|---|---|
| Cardiac surgery | 105.4 | 55.2 |
| General medicine* | 48.6 | 18.1 |
| Cardiology | 34.8 | 48.2 |
| General surgery | 23.7 | 5.4 |
| Neurosurgery | 16.7 | 10.5 |
| Paediatrics | 16.6 | 17.2 |
| Geriatrics | 13.0 | 6.2 |
| Psychiatry | 8.8 | 0.3 |
| Dermatology | 3.6 | 8.7 |
| ENT | 1.3 | 0.5 |
| Neurology | 1.0 | 0.9 |
| Mean | 27.7 | 13.3 |

* General medicine includes rheumatology and renal medicine.

TABLE II

Out-of-hours radiological procedures undertaken August and September 1984

| Procedure | Number | Per cent |
|---|---|---|
| Chest (ward) | 467 | 31 |
| Chest (department) | 459 | 31 |
| Abdomen (department) | 278 | 19 |
| CT | 35 | 2 |
| Abdomen (ward) | 23 | 2 |
| Skull | 22 | 1 |
| IVU | 15 | 1 |
| Cardiac catheterisation | 14 | 1 |
| Other radiographs | 87 | 6 |
| Other "administrative" | 89 | 6 |
| Total | 1489 | 100 |

film, etc.) and the time at which the call started and ended. Summary information about number of units used during August and September 1984 by specialty was obtained from the computerised radiology workload system operating in the same hospital. Revenue costs attributable to the department of radiology, including radiographers' rates of pay for out-of-hours work, were obtained from the Health Authority's Treasurer's department, based on the specialty cost return.

It should be noted that in the hospital studied there is no accident and emergency department and the orthopaedic cases treated are almost entirely from the waiting list.

## Results

There was a substantial variation between specialties in the number of radiological requests per 100 deaths and discharges made out of hours and the proportion of their total radiological units requested out of hours (Table I). The overall rate (requests per 100 deaths and discharges) at which radiological investigations were undertaken out of hours was 27.7, with a 100-fold variation between specialties (Table I). Among these, cardiac surgery is a high-use specialty (more than 90 requests per 100 deaths and discharges) while ear, nose and throat (ENT), dermatology, and neurology are low users (less than 3.6 requests per 100 deaths and discharges).

Overall, 13.3% of all radiographic work units used in the hospital studied were due to out-of-hours radiographs. Cardiology and cardiac surgery used about 50% of their total units out of hours, while neurology, psychiatry and ENT used less than 1%. Specialties were broadly similar in the proportion of patients for whom more than one radiograph was requested, suggesting that a tendency to multiple investigations does not explain the variation shown. Specialties with high out-of-hours usage also tended to have high overall usage.

Table II shows that chest and abdomen radiographs accounted for 82.4% of all procedures undertaken out of hours. The proportion of chest radiographs taken in the department was similar inside and outside normal working hours, but outside normal working hours a relatively greater proportion of all radiological investigations performed were chest radiographs taken on wards and abdomen radiographs performed both in and out of the department. Other relatively common investigations were computed tomography (CT), skull radiography, intravenous urography (IVU) and angiography, which accounted for a further 5.8%. These radiographs accounted for a smaller proportion of the out-of-hours work than that carried out during normal working hours. The 87 other radiographs represented a further 5.8% and "administrative" procedures including "making arrangements", "splicing film", "patient refused examination", etc., comprised the remaining 6%

Neither the total number of patients receiving a radiological examination nor the total number of radiographs taken outside normal working hours showed a significant daily or monthly variation, even in general surgery which takes emergency patients only on certain days of the week. There were marked hourly variations with peaks at 9 a.m. and 2 p.m. on Saturdays (but not Sundays) and at 6 p.m. and 10 p.m. on weekdays (but not at weekends or on a Bank Holiday Monday and Tuesday which occurred during the study period). There was a steep fall in the number of requests after midnight with only 4.5% of all out-of-hours requests being performed between 4 a.m. and 7 a.m.

Table III shows a wide variation in the duration of most investigations, the greatest being for pacemakers and IVUs and the least for skull and ankle radiographs. Radiographic work units are allocated to each investigation according to a standard formula based on the notional time required for a radiographer to complete the investigation (approximately one unit to

TABLE III

DURATION OF RADIOLOGICAL PROCEDURES

| Investigation | Mean (min) | SD (min) | Minimum (min) | Maximum (min) |
|---|---|---|---|---|
| Chest (department) | 13.7 | 5.5 | 3 | 59 |
| Abdomen (department) | 14.4 | 4.1 | 8 | 25 |
| Lumbar spine | 18.7 | 4.6 | 14 | 26 |
| CT | 121.2 | 45.5 | 30 | 195 |
| Cardiac catheter | 101.8 | 56.0 | 45 | 200 |
| Pacemaker | 32.3 | 17.8 | 12 | 54 |
| Chest (ward) | 17.9 | 5.2 | 2 | 46 |
| Abdomen (ward) | 23.2 | 6.3 | 17 | 36 |
| Skull | 18.2 | 2.8 | 16 | 23 |
| IVU | 38.9 | 31.7 | 14 | 122 |
| Ankle | 17.8 | 3.6 | 13 | 21 |

1 min) (DHSS/Welsh Office, 1972). Even the original report on which the allocation of units is based (DHSS/Welsh Office, 1972) acknowledged that this measure, like the others it examined, was approximate and the figures in Table III bear this out. In the case of a pacemaker, one unit is equivalent to a mean of 21 s, whereas one unit is associated with a mean of 2 min 58 s (5.6 times as long) for an ankle radiograph.

A total of £6824 was paid to radiographers for out-of-hours duties during the study period, of which hourly payments accounted for £6102 (89.4%) and stand-by/on-call payments for £722 (10.6%). From the specialty cost return, the emergency duty payments to radiographers in the hospital studied totalled £50 500 in the financial year 1984/85, and for the health authority as a whole £93 300 during the same period

## DISCUSSION

There was a substantial variation in out-of-hours radiology usage between specialties with regard to the total units used, the total number of patients radiographed, the proportion of overall units attributable to out-of-hours investigations, and the requests per 100 deaths and discharges. The association between high out-of-hours use and high overall use suggests that the different types of cases between specialties may explain some of this variation. However, the interspecialty differences are not due to variations in the proportion of patients who receive multiple investigations The differences observed could also be due to differences in established practice for the same condition, or to a difference in the distribution between specialties of doctors who request more radiographs than their colleagues in similar circumstances.

Although a wide range of radiographs is requested outside normal working hours, Table II shows that the performance of out-of-hours radiology services could be studied satisfactorily by looking at chest and abdominal radiographs alone. If CT, skull radiographs, IVUs and cardiac catheterisations are added, almost 94% of all radiological requests would be covered.

The large variation in the time required to perform the investigations shown in Table II has important implications, particularly if clinical budgeting is to be introduced If such budgets require clinicians to "purchase" radiology services, this will probably be on the basis of a standard cost for a unit, the number of units being calculated using a formula which is similar to, or the same as, that currently used. If an audit were to reveal that different specialties cater for types of patient requiring markedly more or less time than the average for particular investigations, charges based on the standard allocation of units will be seriously inaccurate. The efficient use of radiological resources requires that they be quantified as accurately as possible. On the other hand, if the variation is due to variations between individual radiographers, the implications are quite different, though no less important.

The finding of a lack of variation by day and by month runs counter to expectation This relative constancy may indicate that the association between emergency admission and the need for out-of-hours radiographs is weak. It also suggests that the role of the inexperience of junior doctors is less than might have been expected, since this would be expected to result in a higher usage in February and August, when the majority of junior medical staff take up posts.

The fact that 90% of the payments made to radiographers for out-of-hours duties are from hourly claims, which depend directly on the requests made, and only 10% are flat-rate payments implies that reduction of radiographic requests could result in significant financial benefits to the National Health Service (NHS), even if the same flat-rate payments continued to be made in order to maintain the current radiographer staffing levels outside normal working hours. Even if the number of radiographs currently taken were not reduced, but all were performed during normal working hours, the health authority studied might save up to £30 000 per annum, even after allowing for the salaries of additional radiographers to carry out the extra investigations performed during working hours. This might mean a potential saving to the NHS in England and Wales of up to £6 000 000 per annum. In some hospitals, the radiological facilities are already being used at full capacity during normal working hours and the economic implications may therefore be somewhat more complicated than the simple model presented here suggests.

The differences between specialties seem greater than might have been predicted and suggest that it may be useful to examine more closely the reasons why some specialties use so much greater a proportion of their total units outside normal working hours. It is reasonable to explore whether this variation might be reduced since if this were to be possible, substantial savings might result.

Variations in duration suggest that there may be opportunities for improving procedural efficiency. The

NHS is probably spending about £18 000 000 per annum on out-of-hours payments to radiographers, of which only £2 000 000 is for flat-rate payments. This does not include the capital and other revenue costs of the radiographs taken, some of which are undoubtedly higher for radiographs performed outside normal working hours.

As a follow-up to the study described in this paper, an audit of out-of-hours radiographs in a district general hospital is planned. This will investigate the extent to which such radiographs are "administratively" appropriate (*i.e.* whether they could or should be taken during normal working hours) and "clinically" appropriate (*i.e.* whether the radiographs requested reveal information which contribute to clinical decisions). In addition, the routine use of information from forms on which radiographers claim for out-of-hours work as a management tool is being explored.

## ACKNOWLEDGMENTS

The authors wish to thank Mr Alexander Yule for making available the radiographers' data and giving advice on their interpretation and Mr Robert Thatcher of the Management Services Department, South Glamorgan Health Authority, for providing figures on overall radiology use. This work has been made possible by financial support from the Welsh Office.

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1987, *The British Journal of Radiology*, *60*, 557–562 JUNE 1987

# Three-dimensional display of data obtained by single photon emission computed tomography

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(*Received June 1986 and in final form November 1986*)

ABSTRACT

Three-dimensional display of radioactive distributions has been achieved using data generated by single photon emission computed tomography (SPECT) Computer techniques for constructing images are presented and the special problems associated with manipulating SPECT data are reviewed The potential role of three-dimensional imaging in nuclear medicine is discussed and SPECT studies from several illustrative cases are presented.

Emission computed tomography (ECT) has had a wide impact in diagnostic nuclear medicine, allowing improved three-dimensional visualisation of the spatial distribution of uptake of a radiopharmaceutical. Distributions imaged by single photon emission computed tomography (SPECT) are generally constructed in transaxial planes and viewed as contiguous sets of transaxial data or rearranged into sagittal and coronal distributions. It is inevitably difficult to display all reconstructed slices in each orientation simultaneously and it has become common, for example, for the observer to view selected slices with reference to position cursors. For most clinical applications, the advantages of viewing tomographic information are self-evident and outweigh the perceptual disadvantages associated with the need to search through sets of data.

There are several SPECT examinations where viewing the reconstructed data as a three-dimensional (3D) image can be beneficial, especially when the facility to rotate the 3D image or to view inside it is available For example, the detection of a space-occupying tumour usually requires the tumour to be seen in at least two to three contiguous transaxial slices and in sagittal and coronal views. Three-dimensional display, which connects associated structures from contiguous slices, can show the exact location of the tumour in relation to normal structure. Secondly, where a tumour is suspected on the surface of an organ (such as sometimes occurs in the liver), 3D display of the surface might usefully show features which are indicative of abnormal pathology. Thirdly, certain diseases of the liver and kidney are associated with changes in the surface texture of the organ which may be visible on 3D displays (Merrick et al, 1980; Homma & Takenaka, 1985) Fourthly, for diseases (*e.g.* of the thyroid) treated by radionuclide therapy, a knowledge of the functioning volume is desirable (Webb et al, 1986; Ott et al, 1987) and 3D display can act as a guide to selection of the voxels for inclusion in the volume. Finally, conformation radiotherapy might profit from a 3D view of a tumour within normal tissue, and when such a tumour is better visualised from functional imaging than anatomical imaging 3D display of SPECT data could be beneficial.

Three-dimensional display of data from X-ray computed tomography has received much attention (Herman, 1980), finding applications in so-called "non-invasive vivisection". In particular, 3D visualisation of bony structures has proved of use in reconstructive surgery (Gillespie & Isherwood, 1986; Gillespie et al, 1986). Many techniques for 3D display have been developed (Udupa, 1983; Christiansen & Stephenson, 1985) and all require, as the starting point, the input of contours, derived from the tomographic data, which are then linked to generate surfaces. The process of generating contours by thresholding X-ray CT data can be simpler than that for SPECT for several reasons. X-ray CT images are low-noise maps of numbers, linearly related to tissue electron density, with density and spatial resolutions of the order 1% and 1 mm respectively; SPECT images are inherently noisier and of lower spatial resolution (typically 15 mm). Additionally, with the very approximate nature of the techniques for attenuation and scatter corrections, the SPECT data do not relate simply to the radionuclide uptake. Slice widths in SPECT are also generally slightly larger than those in X-ray CT. Consequently, one expects 3D images of SPECT data to have discontinuities with a spatial scale of some 10 mm. Moreover, if it is desired to visualise one structure (such as a tumour) through a second structure (such as an organ surface), difficulties will arise in separately defining the two structures.

For these reasons the 3D display of X-ray CT data is possibly easier when display of bony structure is required In this case it is an easy matter to set a thresholding window to differentiate bone from soft tissue. We would expect, however, that 3D display of soft-tissue structure from X-ray CT data might be more difficult in view of the impossibility of assigning a unique CT signature to each organ. It is precisely this wide dynamic range which makes two-dimensional (2D) X-ray CT so successful with high spatial resolution.

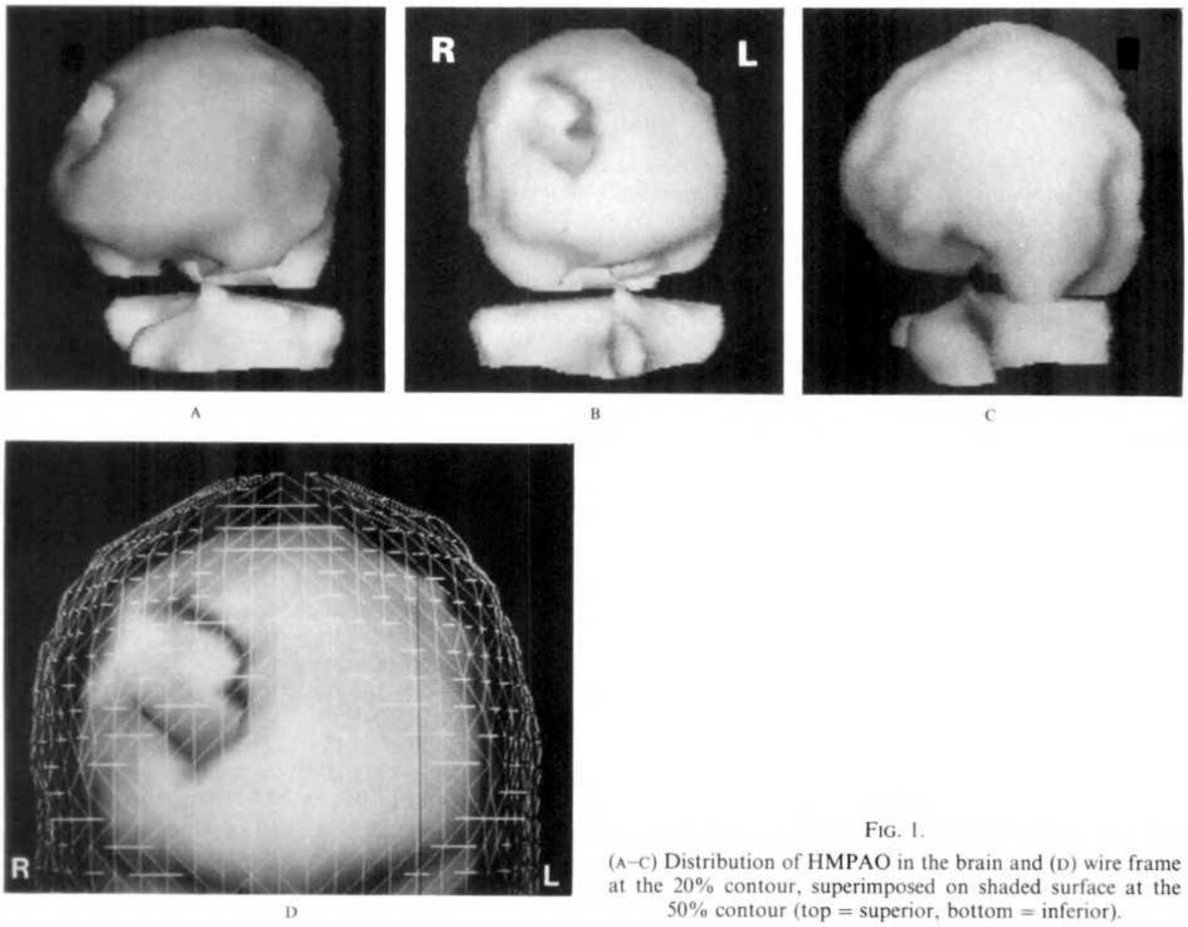


FIG. 1.

(A–C) Distribution of HMPAO in the brain and (D) wire frame at the 20% contour, superimposed on shaded surface at the 50% contour (top = superior, bottom = inferior).

Despite all these difficulties, we have generated 3D SPECT images and are assessing their value. In this paper we report briefly on the methods of construction and follow with examples of what can be achieved.

## METHODS

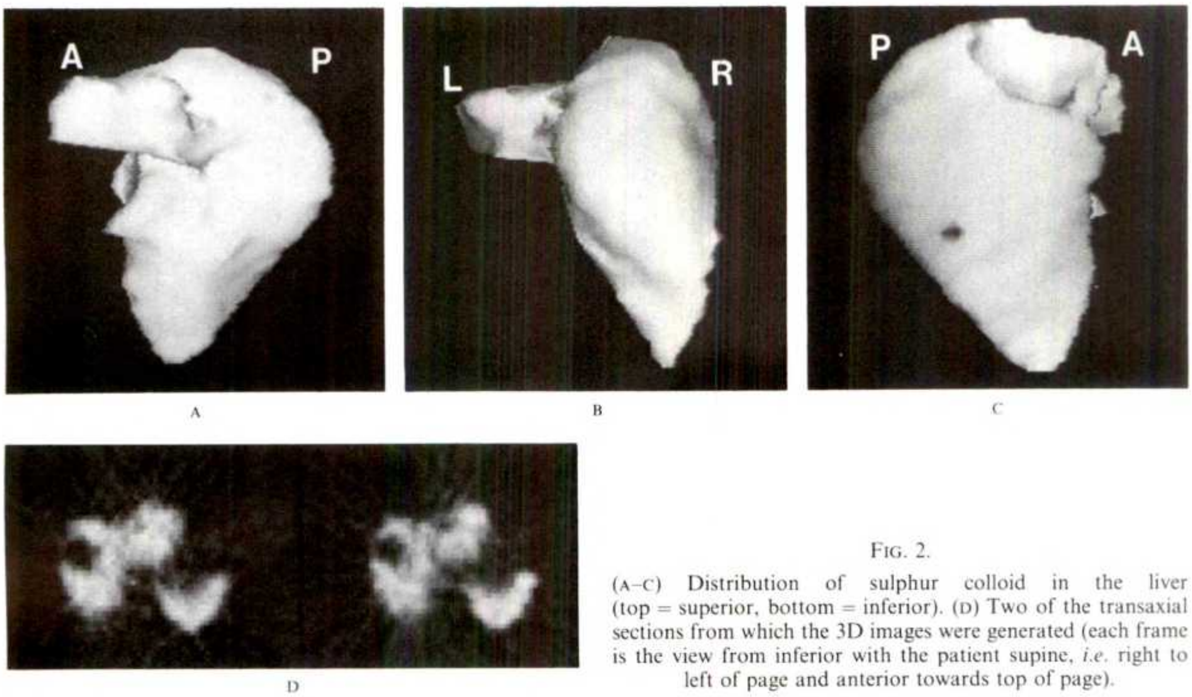
Transaxial SPECT images have been reconstructed on an IGE STAR computer from data acquired by rotating either a GE 400A or a GE STARCAM camera through 360° around the volume of interest. Typically, 64 rotation angles were used with 15 s per view. All images were acquired with $^{99}$Tc$^{m}$-labelled radiopharmaceuticals (for details see illustrative cases below) with a 20% energy acquisition window. Reconstruction was by filtered back-projection.

### *(a) Three-dimensional images based on MOVIE.BYU*

Transaxial data were transferred by magnetic tape to a VAX 750 computer for production and display of 3D images. The entire set of transaxial data were viewed on a SIGMEX ARGS 7000 display and the sections of the volume(s) of interest were contoured at a threshold set by the user. The threshold was varied until the user was satisfied that the structures of interest were properly contoured. The number of structures outlined in each transaxial frame could be varied.

The sets of contours thus produced were submitted to the suite of programs MOVIE.BYU for generating 3D images. MOVIE.BYU is a large, widely distributed 3D imaging package with many features (Christiansen & Stephenson, 1985). In outline, the software first generated a 3D mosaic of tiles which connects the contours. The mosaics can be viewed as "wire-frame" 3D images but were more usually shaded corresponding to the surface reflection of light(s) from specified location(s). The shaded surfaces can be made semi-transparent for the viewing of otherwise hidden internal structures. Images can be produced in grey tones or in colour with different colours ascribed to different parts of a complex 3D structure.

Local software was used to provide a real-time movie of a 3D structure, as seen from a series of contiguous locations around the structure. Rotation can be around any chosen axis but most usefully, following the movements of the gamma camera, around the superior–inferior axis.



A

B

C

D

FIG. 2.

(A–C) Distribution of sulphur colloid in the liver (top = superior, bottom = inferior). (D) Two of the transaxial sections from which the 3D images were generated (each frame is the view from inferior with the patient supine, *i.e.* right to left of page and anterior towards top of page).

Additionally, movies have been constructed at fixed viewing orientation with sequential frames being the shaded surfaces generated at increasing threshold. This mode of display gives a sense of stripping away the outer layers of the radioactive distribution.

*(b) Simple three-dimensional image production*

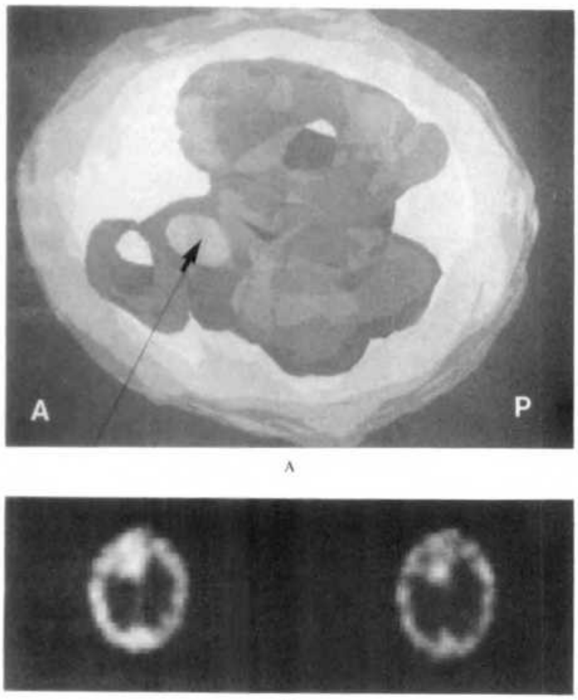
A second method of 3D image production has also been investigated using the VAX computer. The method is based on a technique due to Novak (1986). Similar work has also been reported by Gibson (1983), utilising SPECT data. A viewing position was established such that the transaxial data were viewed edge-on as a stacked set of frames. The frames may be rotated around the superior–inferior axis to establish the viewing orientation and were linearly interpolated from $64^2$ to $256^2$ pixels within each plane. Linear interpolation was also used to create three pseudotransaxial planes between each pair of transaxials. The 3D image was constructed in two stages. Firstly, for each viewing plane pixel, the distance, along the normal to the viewing plane, was computed from the viewing plane to the first pixel whose value lies above a specified threshold, and a value was entered into the view-plane pixel inversely proportional to this distance. This was repeated for all view-plane pixels so that the resulting image was a slowly varying representation of the 3D view from that plane onto a surface of interest in the transaxial set. This image was then used to calculate the vector normal for the surface element at each view-plane pixel and the 3D image was multiplied by a factor which was a power (between 0 and 1) of the surface reflectivity. The image was then smoothed a number of times. The resulting image depicted a shaded surface of the radioactive distribution at a specific threshold level. This technique cannot depict hidden structures nor multiple structures if they physically overlap at a specified single threshold value but the stripping technique described above could be used to reveal inner structures or the inner structures could be examined by selecting a viewing plane within the object. The image is monochrome. Wire frames are not generated as part of the tiling process.

## ILLUSTRATIVE CASES

In this section a series of clinical examples illustrating the use of 3D images is presented. All figures were produced by Method (a) except for Case 6.

### *Case 1*

Figure 1 shows a 3D representation of the uptake distribution of $^{99}$Tc$^{m}$-labelled HMPAO in the brain of a 51-year-old woman who had brain metastases from a small-cell lung carcinoma. The images were produced by thresholding the transaxial data at 50% of the maximum reconstructed pixel value. The distribution is shown from three viewpoints (chosen from a set of 16 used to construct a real-time movie). Also shown is the superimposition of a wire frame at the 20% contour on the shaded surface distribution at the 50% contour. The uptake of HMPAO in the brain and the surrounding tissues can be clearly seen. The inferior surface of the brain with the inferior aspects of the frontal lobes, the temporal lobes and the occipital region can be clearly



A

B

FIG. 3.

(A) Distribution of glucoheptonate in the brain, showing tumour (arrow) (superior to inferior view: right to the top of image, left to bottom). (B) Two of the transaxial sections from which 3D images were generated (each frame is the view from inferior with the patient supine, *i.e.* right to left of page and anterior towards top of page).

identified. In this patient the uptake of HMPAO in the tumour was reduced or absent and this is seen as a cavity in the 3D reconstruction.

*Case 2*

Figure 2 shows the distribution of $^{99}$Tc$^{m}$-labelled sulphur colloid in the liver of a 49-year-old man who had a secondary deposit in the anterior and superior aspect of the right lobe of the liver extending from the surface to a depth of several centimetres. This lesion was a metastasis from a carcinoma of the colon and the 3D image clearly demonstrates the lack of uptake of sulphur colloid in the lesion. The 3D image is a shaded surface at the 35% contour. The posterior views of the liver show the moulding of the liver to the diaphragm and other viscera, while the impression of the spine is clearly visible. Two of the transaxial sections from which these images are produced are shown in Fig. 2B. The transaxial SPECT data naturally show the distribution of activity within the external contour but the contour itself can be better appreciated from inspection of the 3D data.

*Case 3*

Figure 3A shows the distribution of $^{99}$Tc$^{m}$-labelled glucoheptonate in the brain of a 53-year-old man with a bilateral, multicentric glioma. The image shows three separate surfaces: the outer surface of the brain, the inner surface of the ventricles, and the outer surface of the tumour itself. The outer surfaces have been made semi-transparent so that when the total image is rotated the position of the tumour relative to the other structures becomes more evident in 3D space. Figure 3A is a black-and-white print of a colour image in which the three parts of the 3D image were coloured red, blue and yellow. The use of colour makes the separate parts more apparent. Figure 3B shows two of the transaxial sections used to create the 3D display.

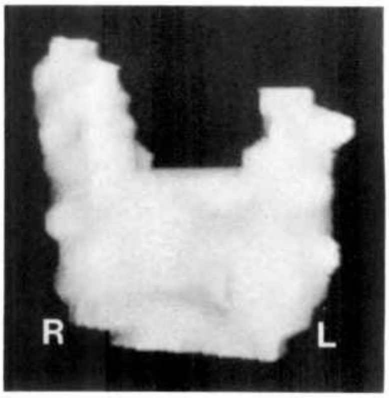


FIG. 4.

Distribution of pertechnetate in the thyroid. (Superior to top.)

*Case 4*

Figure 4 shows the distribution of $^{99}$Tc$^{m}$-labelled pertechnetate in the thyroid gland of a 29-year-old woman. Using a 30% contour, the 3D view of the gland clearly shows its multinodular structure with a non-radioactive area involving the left upper pole. The figure is an anterior view, viewed from slightly to one side, and clearly demonstrates the way the thyroid is wrapped around the trachea posteriorly.

*Case 5*

Figure 5 shows the surface of the kidneys of a 7-year-old boy injected with $^{99}$Tc$^{m}$-labelled DMSA. The difference in size is clearly visible. This patient was being investigated to exclude pylonephritic scarring. Smooth outlines in the 3D view help to exclude this possibility. The child has an ectopic left kidney and rotation of the normal axis of the kidney with the pelvis pointing medially and upwards.

*Case 6*

Figure 6 demonstrates the distribution of $^{99}$Tc$^{m}$-HMPAO in a 55-year-old woman who was referred for brain imaging for suspected secondaries from a small-cell lung carcinoma. Figure 6A was produced by Method (a) and Fig. 6B by Method (b), described earlier. Again, the outline of the cerebral hemispheres is clearly defined and the moulding of the inferior surface to the anterior middle and posterior cranial fossae is clearly seen. Uptake is also seen in the tissues of the maxilla. Method (a) appears somewhat superior to Method (b), in that the surface texture produced by Method (a) is a more realistic expectation from inspection of the transaxial data. Figure 6C shows two of the transaxial sections from which the 3D display was generated. Naturally, the 2D data display the internal as well as the contour information but the contour is more easily visualised in three dimensions.

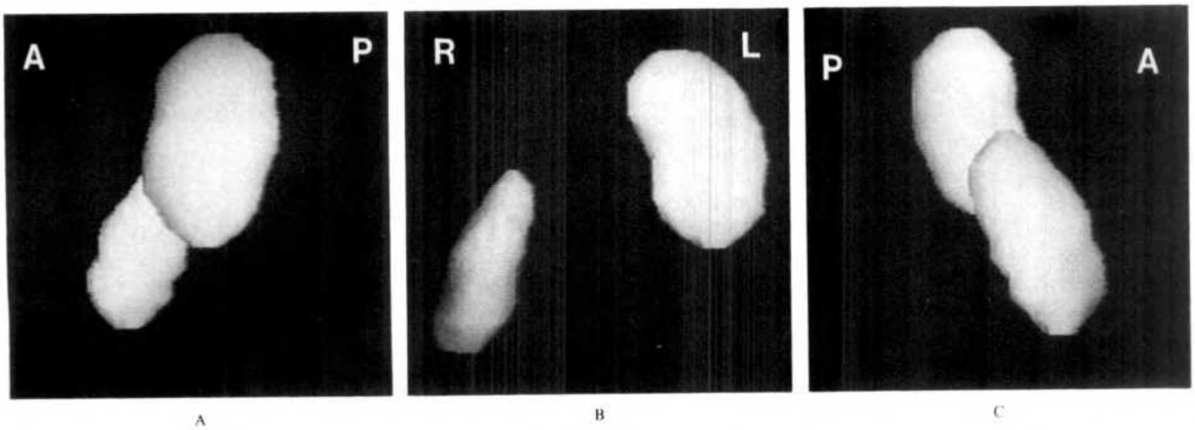


FIG. 5.
(A–C) Distribution of DMSA in the kidney (top = superior, bottom = inferior).

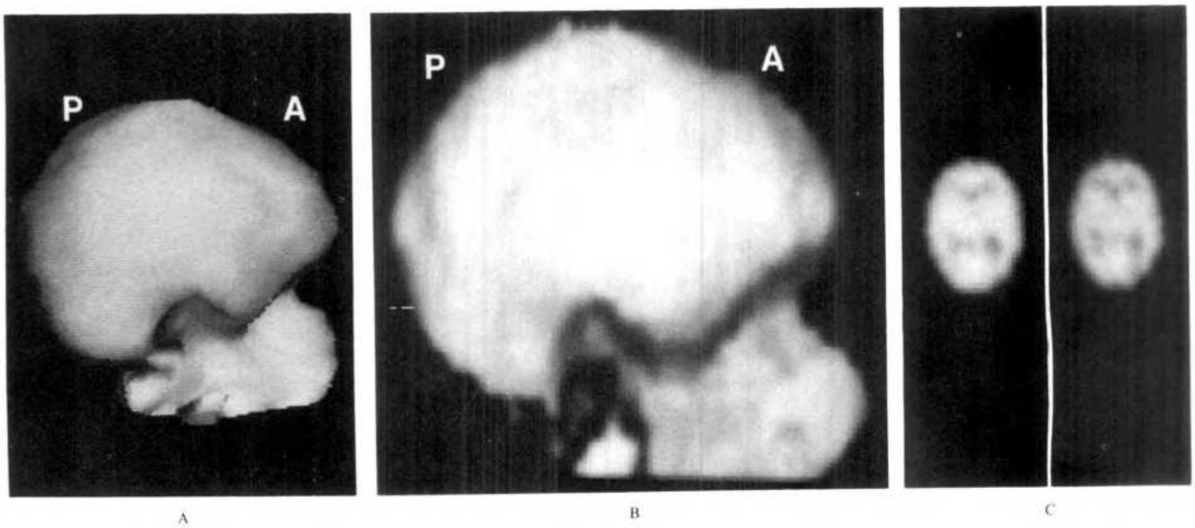


FIG. 6.
Distribution of HMPAO in the brain: (A) image produced by MOVIE.BYU; (B) image produced by Method (b) (top = superior, bottom = inferior). (C) Two of the transaxial sections from which 3D images were generated (each frame is the view from inferior with the patient supine, *i.e.* right to left of page and anterior towards top of page).

## DISCUSSION

The process of generating contours in Method (a) was highly interactive, requiring the user to make decisions on a frame-by-frame basis and to assist the process by making a suitable choice of starting locations for the contour search routines. It would be unrealistic (and undesirable) to seek to automate this process, since the reasons discussed in the introduction necessarily preclude imaging which could be automatically contoured.

The simple Method (b) was developed to assess whether it would be computationally quicker or easier to use than MOVIE.BYU. In practice, computation times were much the same. A possible advantage of this technique is that it requires no interactive decision-making from the user. Stated conversely, this means that no tuning by the user is allowable in order to get the best possible image (other than simple changes of shading parameters). This, together with the lack of features described above (such as simultaneous viewing of surfaces and hidden structure) compared with MOVIE.BYU, leads us to conclude that such techniques are possibly too limited. It is possible that the generation of stripping movies which gradually reveal hidden structures may overcome this deficiency and prove as useful as simultaneous display but, as yet, the relative merits have not been assessed. We are currently assessing commercial software similar to that in Method (b) which allows production of stripping movies (courtesy of IGE). We should make clear, however, that comparisons between the techniques may be somewhat unfair in view of the many man-years of work represented by the package MOVIE.BYU, and further work is needed to ensure that there is justice in the comparison.

From the illustrative cases it is clear that, despite the difficulties, 3D display of SPECT data is possible and can add clarity of interpretation to inspection of sets of tomographic slices. By rotating or stripping the distributions, additional appreciation of 3D structure arises. The processes involved in generating 3D images are complex and are probably not to be undertaken for every case, but should be reserved for those occasions where interpretation is difficult from the corresponding 2D images. The user contributes a measure of interactive decision-making and thus, in a sense, 3D images display what the user chooses to see. For diagnosis they should be viewed alongside the 2D data This is especially important since 3D images contain less information that 2D images, the justification for their production being a potential improved clarity of interpretation.

## ACKNOWLEDGMENTS

We should like to thank Mr R. Clack and Mr A. P Long for assistance with 3D software development associated with implementing MOVIE BYU and Mr R. May for the STAR to VAX transfer software We are grateful for many discussions with Dr R. Bentley concerning display devices.

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# Absorbed dose from $^{14}C$ xylose and $^{14}C$ mannose

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(*Received September 1986 and in revised form December 1986*)

## ABSTRACT

Tissue distribution and excretion studies have been performed in rats and mice for up to 1 week after oral administration of $^{14}C$ xylose and $^{14}C$ mannose. The effective dose-equivalent is calculated to be 15 μSv/MBq for xylose and 120 μSv/MBq for mannose. Since there was no clearance of mannose during the period of the study, the effective dose-equivalent for mannose is almost entirely dependent upon the assumptions made about expected lifetime exposure.

Bacterial colonisation of the small intestine can be detected either directly, by intubation of the jejunum and culture of the aspirate, or indirectly by measurement of gas released during bacterial metabolism of an administered substrate. Direct sampling by intubation is difficult, time consuming and carries a risk of giving false positives as a result of contamination of the small bowel during intubation. Measurement of the concentration of hydrogen in the breath following an oral glucose load (Metz et al, 1976) is a reliable means of detecting colonisation by anaerobic organisms, but in clinical practice carries a 20–30% false negative rate (King & Toskes, 1983). $^{14}C$ xylose is a pentose sugar of plant origin which has been advocated as an alternative breath test substrate (Toskes et al, 1978; King et al, 1979), but suffers from the disadvantage that it undergoes metabolism in the liver after absorption from the small bowel, with the release of $^{14}CO_2$ which cannot be distinguished from that produced by intraluminal bacteria. Mannose is a C6 epimer of glucose which is absorbed from the small intestine much more slowly than xylose, and is not reabsorbed from the renal tubule (Wood & Cahill, 1963). These properties suggest it warrants investigation as a potential diagnostic agent for detecting small-bowel colonisation.

It is in principle possible that $^{14}C$ in any administered sugar could be incorporated into fat or other substances with a long biological half-life. Accurate dosimetry data are therefore essential. There are no published estimates of the absorbed dose likely to result from the use of $^{14}C$ mannose, and published data on xylose dosimetry (King et al, 1980) are unsatisfactory because they are incomplete. We have performed tissue distribution studies of these two sugars in rats and mice in order to estimate the absorbed dose and calculate the effective dose-equivalent.

## MATERIALS AND METHODS

Rats were lightly anaesthetised with ether and a measured dose of the test sugar (20 mg/kg of either mannose or xylose, 10 kBq $^{14}C$ per mg (Amersham International)) instilled into the stomach by orogastric tube. After recovery the animals were placed in metabolic cages. Water was allowed *ad libitum* and food after the first two hours. Urine and faeces were collected separately into alkali to prevent loss of carbon dioxide. The animals were weighed and killed after 2 days and liver, kidney and samples of adipose tissue taken for further analysis.

A similar procedure was followed with mice, with groups of five in each metabolic cage. The animals were weighed before killing at 24 h, 48 h or 7 days, dissected immediately after death and liver, kidneys and a sample of adipose tissue taken as for the rats. The residue of the carcase was homogenised in a liquidiser and a weighed aliquot refrigerated at −20°C for freeze-drying along with other organs. Weighed aliquots of freeze-dried material were oxidised in a stream of oxygen using a Packard 306B sample oxidiser. The $CO_2$ was absorbed in Carbosorb/Permafluor V 8 : 10 and counted in a beta counter with external standardisation quench correction.

## RESULTS

The distribution of residual radioactivity in the rats is shown in Table I and in mice in Tables II and III. The total activity in fat was estimated from the activity per gramme, assuming the same fat to total body weight

TABLE I

DISTRIBUTION OF MANNOSE AND XYLOSE IN RATS

| | Mean (SD) retention at 48 h in whole organ as a percentage of administered activity | |
|---|---|---|
| | Xylose ($n = 6$) | Mannose ($n = 5$) |
| Liver | 1.7 (0.5) | 3.8 (1.7) |
| Kidney | 0.1 (0.02) | 0.16 (0.01) |
| Urine | 35.7 (14.0) | 4.7 (0.8) |
| Faeces | 2.9 (1.0) | 5.9 (0.6) |
| Fat (per gramme) | 0.06 (0.03) | 0.03 (0.03) |

TABLE II

DISTRIBUTION OF XYLOSE IN MICE

| | Mean (SD) retention in whole organ as percentage of administered activity ($n = 5$) | | |
|---|---|---|---|
| | 24 h | 48 h | 7 days |
| Liver | 1.80 (0.33) | 0.94 (0.05) | 0.09 (0.01) |
| Kidney | 0.068 (0.023) | 0.075 (0.007) | 0.02 (0.006) |
| Carcase | 5.64 (1.01) | 4.42 (0.76) | 1.68 (0.17) |
| Urine (pooled) | 34.0 | 43.0 | 41.0 |
| Faeces (pooled) | 3.5 | 5.1 | 3.4 |
| Fat (per gramme) | 0.09 (0.03) | 0.24 (0.05) | 0.13 (0.03) |
| Fat (total) | 0.40 (0.13) | 1.08 (0.23) | 0.44 (0.10) |
| Weight of animals (g) | 25 (3) | 25 (1) | 19 (5) |

TABLE III

DISTRIBUTION OF MANNOSE IN MICE

| | Mean (SD) retention in whole organ as percentage of administered activity ($n = 5$) | | |
|---|---|---|---|
| | 24 h | 48 h | 7 days |
| Liver | 2.2 (0.6) | 1.1 (0.3) | 0.22 (0.04) |
| Kidney | 0.17 (0.03) | 0.14 (0.02) | 0.05 (0.01) |
| Carcase | 5.9 (0.9) | 4.7 (0.7) | 2.3 (0.8) |
| Urine (pooled) | 4.4 | 4.4 | 5.1 |
| Faeces (pooled) | 4.2 | 4.4 | 4.2 |
| Fat (per gramme) | 0.23 (0.10) | 0.17 (0.07) | 0.29 (0.15) |
| Fat (total) | 1.11 (0.48) | 0.91 (0.37) | 1.14 (0.59) |
| Weight of animals (g) | 27 (2) | 30 (2) | 22 (4) |

ratio as standard man (Snyder et al, 1975). The initial activity and the half-life in each organ was estimated by fitting the concentrations to a single exponential and extrapolating to zero time. The effective life for each organ was calculated by multiplying the half-life by 1.44 The concentration in adipose tissue after mannose showed little variation over the 7 days of the study and was regarded as constant. The average value was used in the calculation of absorbed dose. The concentration in adipose tissue after xylose showed a significant increase during the first 2 days, followed by a significant clearance. The rate of clearance between Days 2 and 7 was used in the dose calculation. Although more than half of both sugars was not accounted for and is therefore assumed to have been exhaled, the absorbed dose to the lung was not calculated separately because the residence time in the lungs was too short to measure by the techniques employed.

Organ doses were calculated using the standard MIRD methods (Snyder et al, 1975). The highest activities observed in pooled urine and faeces over the period of the study were used to calculate the radiation doses to the bladder and lower large intestine. Tables II and III indicate that there was unlikely to be any additional urinary or faecal excretion beyond this time. The effective dose-equivalent (EDE) was calculated using International Council on Radiological Protection (ICRP) risk weighting factors (ICRP, 1977). This provides a single dose value which takes into account the non-uniform distribution and effects of a particular radiopharmaceutical. Although not the originally intended use of EDE, it is now accepted by the UK licensing authorities as a useful risk estimate. The results are summarised in Tables IV and V.

## DISCUSSION

Relatively little is known about the radiation dosimetry of $^{14}C$ sugars. Most calculations derive from measurements of exhaled or urinary activity and the distribution of the residue was assumed to be uniform (Tolbert & Cozzetto, 1963). The possibility of incorporation into slowly turning over compartments has not previously been tested. No information exists

TABLE IV

ABSORBED DOSES FOR XYLOSE IN MAN CALCULATED FROM THE ANIMAL DISTRIBUTION DATA BY THE STANDARD MIRD METHOD

| Organ | Weight, g | Effective life ($T_E$), h | Initial activity, % | Absorbed dose per unit accumulated activity ($S$), μSv/MBq/h | Mean absorbed dose ($D$), μSv/MBq | Weighting factor | Effective dose-equivalent, μSv/MBq |
|---|---|---|---|---|---|---|---|
| Gonads | 60 | 120 | 0.0058 | 811.0 | 5.64 | 0.25 | 1.41 |
| Breast | 350 | 120 | 0.034 | 1.0 | 0.04 | 0.15 | 0.01 |
| Red bone marrow | 1500 | 120 | 0.145 | 17.8 | 3.10 | 0.12 | 0.37 |
| Thyroid | 20 | 120 | 0.0019 | 1432.0 | 3.26 | 0.03 | 0.10 |
| Trabecular bone | 1000 | 120 | 0.096 | 1.7 | 0.20 | 0.03 | 0.01 |
| Liver | 1800 | 49 | 2.73 | 15.7 | 21.00 | 0.06 | 1.26 |
| Kidneys | 310 | 107 | 0.098 | 91.9 | 9.64 | 0.06 | 0.58 |
| Adipose tissue | 12 500 | 135 | 1.52 | 1.0 | 2.05 | 0.06 | 0.12 |
| Bladder | – | 4* | 43† | 70.3 | 120.92 | 0.06 | 7.26 |
| Lower large intestine | – | 12* | 5.1† | 105.4 | 64.50 | 0.06 | 3.87 |

Effective dose-equivalent = 15.0 μSv/MBq

*Mean residence time.
†Total activity.

TABLE V

ABSORBED DOSES FOR MANNOSE IN MAN CALCULATED FROM ANIMAL DISTRIBUTION DATA USING THE STANDARD MIRD METHOD

| Organ | Weight, g | Effective life ($T_E$), h | Initial activity, % | Absorbed dose per unit accumulated activity ($S$), μSv/MBq/h | Mean absorbed dose ($D$), μSv/MBq | Weighting factor | Effective dose-equivalent, μSv/MBq |
|---|---|---|---|---|---|---|---|
| Gonads | 60 | 157 | 0.0057 | 811.0 | 7.26 | 0.25 | 1.82 |
| Breast | 350 | 157 | 0.033 | 1.0 | 0.05 | 0.15 | 0.01 |
| Red bone marrow | 1500 | 157 | 0.142 | 17.8 | 3.97 | 0.12 | 0.48 |
| Thyroid | 20 | 157 | 0.0019 | 1432.0 | 4.27 | 0.03 | 0.13 |
| Trabecular bone | 1000 | 157 | 0.095 | 1.7 | 0.25 | 0.03 | 0.01 |
| Liver | 1800 | 66 | 2.73 | 15.7 | 28.29 | 0.06 | 1.70 |
| Kidneys | 310 | 117 | 0.21 | 91.9 | 22.58 | 0.06 | 1.35 |
| Adipose tissue | 12 500 | 175 200 | 1.05 | 1.0 | 1839.6 | 0.06 | 110.4 |
| Bladder | – | 4* | 5.1† | 70.3 | 14.34 | 0.06 | 0.86 |
| Lower large intestine | – | 12* | 4.4† | 105.4 | 55.65 | 0.06 | 3.34 |

Total effective dose-equivalent = 120 μSv/MBq

*Mean residence time.
†Total activity.

regarding species differences in the way these compounds are treated. Thus, the finding of an appreciable difference in the fat content after 48 h in two rodent species indicates that absorbed dose estimates based on data derived from a single small mammalian species must be treated with some caution. Based on experience with other compounds it is likely to err on the side of overestimating the dose.

Very little $^{14}C$ was found in the faeces of either species, whichever sugar was administered. Recovery was virtually complete within 24 h. As expected, the amount of xylose recovered from the urine was much greater than that of mannose, urinary recovery of mannose being similar to the faecal recovery. In view of the large discrepancy between the total recovered and the amount given, it is evident that over 50% of the administered activity of both sugars was exhaled in both species.

The difference in effective dose-equivalent between the two sugars is explained by the difference in half-life of activity incorporated into tissue, especially fat. This was relatively short after administration of xylose but so long with mannose that no turnover could be measured in the period of the study. For the purpose of calculating absorbed dose it was taken as 20 years. This assumes that there is *no* subsequent clearance from adipose tissue so that the period of 20 years represents the average lifetime exposure for a middle-aged patient. Since this component dominates the total effective dose-equivalent it would have to be modified according to the age of the patient. It is evident that, in the mouse, substantially more of the $^{14}$C from mannose than from xylose is incorporated into products which turn over slowly. Thus, despite poor absorption, it cannot be assumed that any $^{14}$C-labelled sugar is totally unmetabolised. However, even with mannose, and making extremely conservative assumptions about turnover, the effective dose-equivalent is such that the clinical administration of quantities sufficient for a breath test to be performed is not precluded

AKNOWLEDGMENTS

We would like to express our thanks to Inveresk Laboratories Ltd for allowing us to use their sample oxidiser and to Mrs J Robertson and the staff of the Animal Unit, Western General Hospital for their assistance

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1987, *The British Journal of Radiology*, 60, 567–578 JUNE 1987

# Limitations to the killing of tumours using radiolabelled antibodies

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(*Received October 1986 and in revised form January 1987*)

ABSTRACT

We have calculated the minimum requirements for effective therapy using intravenously administered, tumour-directed antibodies labelled with either iodine 131 or yttrium 90. A lethally large amount of either radionuclide would be required to achieve tumour destruction. At least a 10-fold increase in tumour uptake is necessary to combine tumour destruction with a survivable whole-body dose. The required improvement in specific uptake can be substantially reduced by accelerating the excretion of radioactivity outside the tumour. For all situations studied, yttrium 90 is superior to iodine 131 as a cytotoxic label.

There is considerable interest in the localisation and killing of tumours using labelled antibodies (Bloomer et al, 1985; Larson, 1985). Most studies have been concerned with localisation, as this is an essential prerequisite to tumour killing. This is reasonable since antibodies that can successfully localise tumours in scanning are also likely to be useful for tumour killing. Unfortunately, in spite of the early promise, there has been little improvement in the sensitivity of the scanning technique (Goldenberg et al, 1978; Goldenberg et al, 1983). There are many reasons for this, including low uptake of the antibody by the tumour and high count rates from non-tumour locations. Many of the parameters involved can be modelled mathematically, allowing a useful assessment of those factors which could lead to improvement in scan quality (Bradwell et al, 1985).

Because the situation is somewhat different for tumour killing, the same models cannot be applied. The parameters are also different if the cells are to be destroyed with radiation, rather than with biochemicals such as ricin (Gilliland et al, 1980; Ettinger et al, 1982). It is not clear which of these techniques will eventually prove successful but there are arguments in favour of radiolabels. Radiation will penetrate areas that are poorly vascularised, the doses required may be derived by reference to other forms of internal radionuclide therapy or brachytherapy, and the kinetics of antibody movement may be determined from scan data. In contrast, drug-labelled antibodies require good tumour blood supply, they may need to enter the cells to be effective and the dose required is not well established.

The purpose of this paper is to analyse the data available on the distribution and uptake of radiolabelled antibodies, and their fragments, and use these to calculate the limiting factors. In order to predict the clinical potential of radiolabelled antibodies, it is essential to combine the known distributions of antibodies with the probable dose and dose rate required for successful treatment (Ellis, 1968). This might allow rational strategies for improving the technique for eventual clinical use.

## PARAMETERS USED IN THE CALCULATION

We have made the following assumptions in the construction of this model.

1. A dose of 60 Gy must be given in 1 week to achieve tumour sterilisation (Ellis, 1968).
2. After injection the radioactivity is evenly distributed such that the body is uniformly irradiated with beta particles. This is not necessarily equivalent to the establishment of an equilibrium between the blood pool and extravascular space.
3. Tumour uptake of activity and elimination from both the tumour and whole body are assumed to follow first order kinetics, as shown in Fig. 1.

The baseline parameters involved in the calculation are taken from reported clinical studies as required and are shown in Table I.

The following parameters are used in the model, including kinetic and uptake values summarised from Table I.

1. Injected activity ($A$ MBq).
2. The percentage, $B$, of the injection available to the tumour.
3. Maximum percentage of injection per gram of tumour (0.005%).
4. Uptake rate of the radiolabelled antibody into the tumour ($k_1 = 2\ \text{day}^{-1}$).
5. Loss of activity from the tumour ($k_2 = 0.23\ \text{day}^{-1}$ iodine 131; no loss of yttrium 90 (Fairweather et al, 1983)).
6. Loss of activity from the body ($k_3$ = values as for Parameter 5).
7. Decay constant of antibody labels ($\lambda = 0.086\ \text{day}^{-1}$ iodine 131; $0.256\ \text{day}^{-1}$ yttrium 90).

The calculation utilises these data to determine the amount of radiolabelled antibody required to deliver the 60 Gy dose. Carrying out the calculation in this way

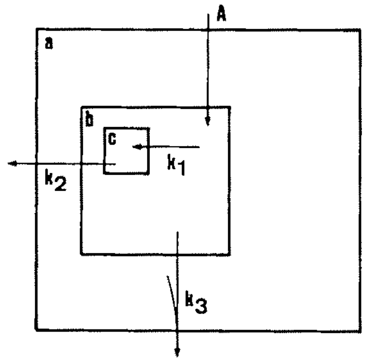

FIG 1.

Schematic diagram illustrating the parameters used in calculating the tumour and whole-body doses. Activity ($A$) labelled to antibody is injected into the blood pool (b) and some percentage ($B$) is available for binding to the tumour (c) at an uptake rate of $k_1$. Activity bound to the tumour is eliminated with a rate constant $k_2$ Activity within the blood pool (b) is in dosimetric equilibrium with the body space (a) and both are eliminated from the body with a rate constant $k_3$

allows the dosimetry to normal tissues to be predicted in the context of a potential tumour cure.

## CALCULATION OF DOSE

$B$ is determined by solving the differential equation:

$$\mathrm{d}B/\mathrm{d}t = -(k_1+k_3)B \qquad (1)$$

Hence at time $t$ days, $B$, the percentage of activity available to the tumour, is related to its value $B_0$ at $t = 0$ by the following equation:

$$B = B_0 \exp.-(k_1+k_3)t\ \% \qquad (2)$$

The percentage, $C$, of activity bound per gram, in a tumour of mass $m$, g, is derived from both tumour uptake and loss of activity and may be obtained by solving the equation:

$$\mathrm{d}C/\mathrm{d}t = \frac{k_1 B}{m} - k_2 C \qquad (3)$$

Hence the percentage $C$ of activity per gram of tumour at time $t$ is:

$$C = \frac{B_0 k_1(\exp.-(k_1+k_3)t - \exp\ -k_2 t)}{m(k_2-k_1-k_3)}\% \text{ per g} \qquad (4)$$

Specifically, the equation is solved to find the time of maximum tumour uptake. The value of $B_0$ is then assigned such that the required maximum percentage uptake (*i.e.* 0.005% of injection per gram) occurs at this time. With this value of $B_0$ Equation 4 is then used to calculate $C$, the percentage activity per gram of tumour at any time $t$

Thus, the activity, $Y$, per gram of tumour at time $t$ can be derived from Equation (4) and is given by:

$$Y = \frac{A}{100}\frac{B_0 k_1}{m(k_2-k_1-k_3)}(\exp.-(k_1+k_3)t - \exp.-k_2 t)\exp.-\lambda t \text{ MBq g}^{-1} \qquad (5)$$

The tumour dose rate can then be obtained by multiplication of Equation (5) by a dose-rate factor for the individual radionuclide in Gy $\mathrm{h}^{-1}$ $\mathrm{MBq}^{-1}$. This is derived from standard texts (Lederer et al, 1967; Snyder et al, 1978).

The whole-body activity, $W$, is:

$$W = A \exp.-(k_3+\lambda)t \text{ MBq} \qquad (6)$$

The dose rate to the whole body may then be derived as above for a body mass of 70 kg.

TABLE I

TUMOUR UPTAKE AND KINETICS OF RADIOLABELLED ANTIBODIES IN MAN

| Study | No of patients | Tumour type | Time* (days) | % of injection per gram tumour ($\times 10^{-3}$) Mean (range) | Half-time for excretion (days). Mean (range) | |
|---|---|---|---|---|---|---|
| | | | | | Tumour | Whole body |
| Allum, 1986 | 7 | Gastric | 3 | 4.3 (1.3–8.8) | N/A | N/A |
| Allum, 1986 | 2 | Oesophageal | 3 | (1.2–3.3) | N/A | N/A |
| Allum, 1986 | 7 | Colorectal | 3 | 4.4 (1.0–7.6) | N/A | N/A |
| Burraggi et al, 1985 | 6 | Melanoma | N/A | 3.0 (0.9–7.0) | N/A | N/A |
| Burraggi et al, 1985 | 8 | Various | N/A | N/A | N/A | 4.8 (3.4–8.0) |
| Farrands et al, 1982 | 2 | Colorectal | 2 | 5.0 | N/A | N/A |
| Larson et al, 1983 | 2 | Melanoma | 3 | (5.7–10) | N/A | N/A |
| Leichner et al, 1983 | 4 | Hepatoma | N/A | N/A | 7.4 (6.7–7.8) | 3.6 (2.9–4.3) |
| Leichner et al, 1983 | 5 | Hepatoma | N/A | N/A | 2.9 (1.9–4.2) | 2.7 (1.4–3.6) |
| Leichner et al, 1983 | 10 | Hepatoma | N/A | N/A | 4.6 (3.9–5.4) | 3.5 (3.3–4.2) |
| Mach et al, 1980 | 3 | Colorectal | 7, 3, 6 | 2.6 (1.2–3.8) | N/A | N/A |
| Mach et al, 1981 | 3 | Colorectal | 6, 8, 4 | 2.6 (1.9–3.9) | N/A | N/A |

* Time from injection to tumour activity assay

N/A Information not available.

The actual tumour irradiation is the sum of the dose rate from the radiolabelled antibody in the tumour, from Equation (5), and the contribution from the uniform whole-body irradiation as derived from Equation (6). The total dose to the tumour or the whole body can be obtained by integration of the dose rate over a specified time, *e.g.* 7 days. The model can also be used to assess the effect of varying the different parameters. In this respect there are three useful questions to ask.

(1) What is the tumour uptake of labelled antibody that gives a tumour-killing dose but spares normal tissue? In this case we have placed an upper limit of 2 Gy on the whole-body dose as a survivable insult without bone marrow rescue (Lushbaugh & Comas, 1967). This balance of dose delivery we have called the therapeutic effect.

(2) What are the effects of different sized molecules, such as antibody fragments, on the required therapeutic effect? The data in the literature show, in animals, both enhanced (Buchegger et al, 1983) and reduced (Ballou et al, 1985; Maillet et al, 1985) uptake of radiolabelled fragments into tumours compared with the uptake of intact antibody molecules. All studies, however, agree that in animals and man fragments are eliminated from the body at a faster rate than that of whole antibody (Burraggi et al, 1985; Pimm et al, 1985).

(3) What possible improvements may usefully be made to increase the therapeutic effect? Examples would be the accelerated uptake of antibody or the enhanced clearance of unbound activity, although the former is preferable since the latter has an associated waste-disposal problem.

## RESULTS

A tumour which does not selectively concentrate antibody will receive the same dose as the body itself. This corresponds to 0.0014% of the injection per gram of tissue for a uniform distribution of activity throughout a body weight of 70 kg. To achieve a tumour uptake of 0.005% per gram requires a 3.6-fold specific accumulation of activity into the tumour. With 0.005% of an injected dose of iodine 131 antibody per gram of tumour, a tumour dose of 60 Gy in 1 week will be associated with a whole-body dose of 17 Gy (Fig. 2). Further reductions in whole-body dose require a substantial improvement in tumour uptake as the tumour dose becomes increasingly dependent on the targeted tumour activity. In order to reduce the whole-body dose to 2 Gy while maintaining the tumour dose, an 11.6-fold increase in the maximum activity within the tumour is required. This corresponds to 58 Gy of the total tumour dose being delivered by antibody. For yttrium 90 a similar calculation indicates that a tumour dose of 60 Gy would deliver 14.8 Gy to the body; 9.6 times more activity is required in the tumour to limit the whole-body dose to 2 Gy. Without any improvement in uptake, the 60 Gy tumour dose would require the injection of 99 GBq (2.67 Ci) of iodine 131 labelled antibody, or 25 GBq (0.67 Ci) of yttrium 90.

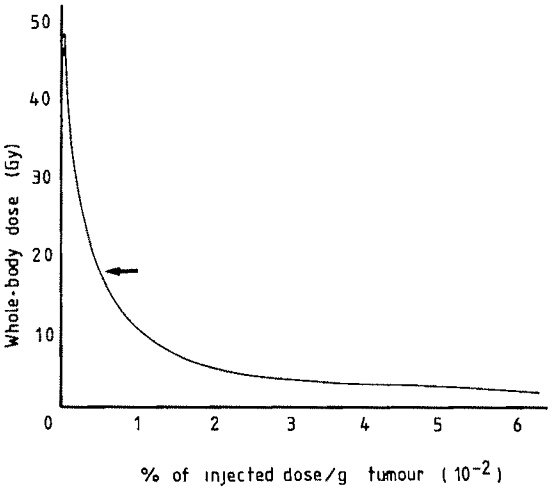

FIG 2.

The effect of specific tumour uptake of iodine-131 antibody on the whole-body dose, consistent with a tumour dose of 60 Gy in 1 week The arrow marks the currently attainable tumour uptake

Retention of all baseline parameters but increasing the uptake rate $k_1$ into the tumour, from a half-time of 8 h to 10 min, reduces the whole-body dose by 10% for yttrium 90. Conversely, the whole-body dose from accelerated uptake of iodine 131 is 14% more, as the maximum tumour activity is rapidly obtained but is then subject to excretion according to the rate constant $k_2$ for tumour elimination. Complete retention of iodine activity by the tumour, but retaining the normal pattern of whole-body excretion, allows a 22% reduction in the whole-body dose.

An enhanced therapeutic effect can be obtained by increasing the elimination rate of activity from the body, thus leading to a lower whole-body dose for both radionuclides (Fig. 3). For example, changing the half-time for elimination of activity from the body from 3 days to 1 day will halve the whole-body dose from yttrium 90 treatment if the tumour uptake is unaffected.

## DISCUSSION

The values we have used to calculate the tumour and whole-body doses are based on data from clinical studies of intravenously administered antibodies reported in the literature. Estimates of whole-body clearance kinetics can be accurately made; less straightforward are determinations of tumour clearance rates where repetitive gamma-camera scans are carried out over the proposed tumour area. Leichner et al (1983) quote errors of at least 15–20% in their analysis of tumour clearance of radiolabelled antibody. The values of

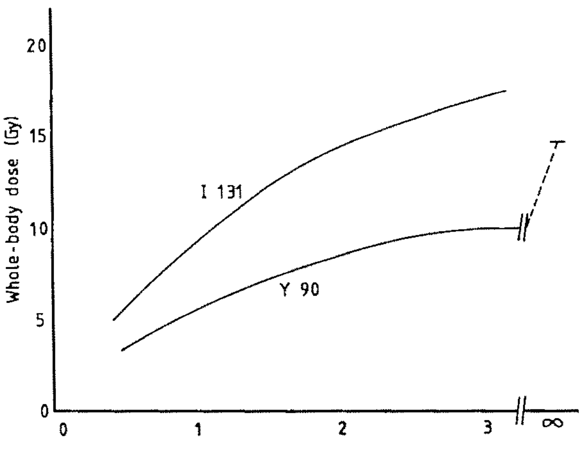

Fig. 3

The relationship between the half-time for elimination of activity from the body and whole-body dose, consistent with a tumour dose of 60 Gy in 1 week

tumour activity are surprisingly consistent but, as can be seen from Table I, these are taken at various periods after injection and each may have contained more activity at an earlier time. Also, tumours extracted some days after the initial injection will contain a variable amount of non-specific activity from the blood and extravascular space. Both these factors were considered in arriving at the figure for tumour uptake of 0.005% of the injection per gram of tumour. This level of tumour uptake is reached approximately a day after injection when used with the baseline kinetic parameters presented in Methods. We believe the values taken for tumour uptake and antibody kinetics represent the best estimates currently available. Other calculations in the literature have been based on animal studies or consider the characteristics only of the radionuclide and tumour (Wessels & Rogus, 1984; Humm, 1986) Such work allows a comparison of various antibodies or nuclides, but does not give any indication of the potential clinical effect of such treatment. It is clear that the literature does not contain sufficient data to support a model of any greater complexity. Such data need to be collected so that a more accurate assessment of dosimetry can be made.

Using the available data, at least a 10-fold increase in specific tumour uptake is needed to make antibody targeted therapy clinically possible In Fig. 2 the whole-body dose received during a 60 Gy tumour irradiation is compared with the percentage of the injection per gram of tumour. The marked position indicates the present levels of antibody uptake within tumours; here a third of the tumour dose is received from unbound antibody Antibody-mediated tumour therapy is dependent upon achieving a tumour uptake that corresponds, in our model, to at least 0.05% of the injection per gram of tumour.

The main disadvantage of our model is that it assumes a uniform distribution of whole-body dose. Radionuclides that are selectively concentrated will have a higher local toxicity which is not included in these calculations. For instance, iodine 131 will contribute a substantial dose to the bladder as a consequence of excretion, while yttrium 90 is selectively concentrated in the liver after injection as a labelled antibody (Hnatowich et al, 1985b; Vaughan et al, 1985) Therefore the model may underestimate the degree of improvement required.

Choice of the administered tumour dose has been based upon typical doses used for intracavitary therapy, as applicable to cervical carcinoma. This treatment delivers 60 Gy in 1 week at a dose rate of 35.7 cGy h$^{-1}$ Using iodine 131 labelled antibodies, the maximum dose rate to the tumour will be 65.7 cGy h$^{-1}$, falling to 10.8 cGy h$^{-1}$ 1 week after injection. The effect of this dose-rate change is not accurately known, though studies using iodine 131 to treat iodine-concentrating thyroid carcinoma have shown that 80–300 Gy is required for sterilisation of this particular tumour (Maxon et al, 1983). Other authors have proposed 80 Gy as a target dose to be achieved by antibody therapy (Humm, 1986). It is well known that reduced dose rates require a greater total dose to sterilise tumour and normal cells; the 60 Gy dose we quote must be taken as a minimum value.

An increase in specific tumour uptake is the most direct method of improving this technique, but it is not yet known how to achieve this. However, there are aspects of antibody targeting which have potential for less substantial improvements. For all possibilities considered here, yttrium 90 is superior to iodine 131 as a radiotoxic label. This is because of the longer residence of metallic ions in the tumour (Fairweather et al, 1983) and the favourable decay characteristics of yttrium 90 The higher energy output from yttrium 90 per decay compared with iodine 131 requires less yttrium 90 activity to be injected to achieve the same tumour dose. The gamma-ray emission from iodine 131 does, however, allow an assessment of the tumour location before and during therapy. This is not possible for the pure beta emitter yttrium 90, but such information may be gained using the antibody labelled with a gamma-emitting isotope of yttrium, such as yttrium 87/87m

The calculation of the likely therapeutic effect of radiolabelled F(ab)$_2$ or Fab fragments is constrained by the lack of quantitative data from clinical studies. All reports agree that the clearance of the antibody fragments is faster than that of intact antibody. However, activity from fragments labelled with indium 111 is eliminated only slowly, presumably as a specific consequence of the dissociation of indium 111 from the fragment (Hnatowich et al, 1985a) Calculations based on the same tumour uptake and retention as that seen with intact antibody show an enhanced therapeutic effect because of a lower whole-body dose. Any reduction in the tumour concentration of activity, or acceleration in the release from the tumour site, will reduce this therapeutic advantage.

Manipulating the excretion rates of the radionuclides themselves may influence the therapeutic effect. For iodine 131 this would be difficult to achieve. Possibly the chemical characteristics of yttrium 90 allow an alteration of its biological distribution. For example, chelating agents can mobilise bound activity and so lead to faster excretion (Vaughan et al, 1987). Also, chelation therapy has been successfully used to remove iron for the treatment of iron storage disease and for the removal of accidentally ingested transuranic elements (Halliday & Powell, 1982; Kalkwarf et al, 1983). If administered chelates do not extract activity from antibody, then the kinetics of antibody uptake into the tumour will not be affected. The removal of a radiolabel may also be achieved by the administration of a clearing second antibody directed against the first (Goodwin et al, 1984). In this case the resultant immune complex is absorbed by the reticuloendothelial system and may subsequently be degraded with the elimination of the label. The second antibody technique is most effective at removing blood-borne, potentially tumour-reactive material, although extravascular sites are poorly cleared The redistribution of activity which will occur with both techniques must be assessed in terms of both tumour dose and dose to the critical normal tissues. For example, second antibody administration will deposit activity into tissues rich in Fc receptor bearing cells, such as the bone marrow. After catabolism of antibody, or chelate treatment, the bladder would receive the majority of mobilised radionuclide

The model presented here allows a quantitative assessment of the problems against which a solution must be evaluated. This will principally depend upon solving the biological restrictions of antibody uptake. Tumour localisation is thought to be limited by circulating antigen, tumour access, antibody binding affinity and many other factors (Bradwell et al, 1985). Major improvements are likely to result only from detailed investigation of these many parameters.

## ACKNOWLEDGMENT

This work was supported in part by grants from the Cancer Research Campaign, UK.

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# Dose-rate effects in normal and malignant cells of human origin*

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(*Received September 1986 and in revised form January 1987*)

ABSTRACT

Human cell lines derived from normal tissue and malignant tumours were irradiated in plateau phase under acute (81 Gy/h) or protracted (0.1–0.7 Gy/h) exposure to determine initial survival curve slopes, assess sublethal damage repair (SLDR) capability, and establish differences in survival due to SLDR over a range of dose rates. No correlation was found between clinical resistance of the tumor types and initial slope or survival at 2 Gy. Sublethal damage repair was assessed by comparing survival curves for acute and continuous irradiation. All cell lines showed significant SLDR, with the more clinically resistant tumour types demonstrating the best recovery rates. The survival data also demonstrated little difference in cell killing over the 0.1–0.7 Gy/h range. Using a modified linear-quadratic model with provisions for SLDR, it was found that for these cell lines the repair half-time was less than 1 h, with no significant change in the amount of recovery from sublethal damage at dose rates below 1 Gy/h.

Malaise et al (1986) studied a large number of cell lines of human tumour origin and demonstrated that the initial portion of the radiation survival curve was the only measure of *in-vitro* radiosensitivity which correlated with the clinical radiosensitivity for various histological tumour types from which the cells originated. They used the $\alpha$ term of the linear-quadratic model, the mean inactivation dose, and $S_2$, the surviving fraction at 2 Gy, to describe the initial part of the survival curve. Preliminary results by Brock et al (1986) with freshly explanted tumour cells also tend to show that cell killing *in vitro* by a dose of 2 Gy correlates with the clinical radiosensitivity of the tumour type. Both studies, however, only showed correlation trends with considerable overlap in cell survival among the different histological groups.

The accuracy of assessing survival after low doses is limited. After 2 Gy, surviving fractions for all cell lines will be within a relatively narrow range (0.2–0.9), making differences between cell types relatively small in relation to experimental error. As discussed in detail elsewhere (Hall & Zaider, 1985), the interpretation of the data in terms of, say, the linear-quadratic model has its own objectional features, among them the fact that the value of $\alpha$ depends critically on the survival data as a whole since $\alpha$ and $\beta$ (the coefficient of the quadratic term in dose) are inversely correlated.

An alternative method of determining the initial slope of the survival curve is to use survival data from low dose-rate continuous irradiation. This approach is based on the assumption (verified experimentally, *e.g.* Hall & Bedford, 1964) that in the survival mechanism, lesions originating from independent energy deposition events (and represented by $\beta D^2$) become increasingly infrequent as the average time between such events (*i.e.* the dose rate) decreases. This phenomenon, attributed to sublethal damage repair (SLDR), can be formally described by

$$S(D) = \alpha D + q(t_0/T)\beta D^2 \qquad (1)$$

where it is explicitly shown that the function q correcting for the SLDR depends only on the ratio $t_0/T$ between the recovery constant $t_0$ and exposure time $T (R = \text{dose rate} = D/T)$. The function q is mathematically identical to the G function, originally proposed by Lea and Catcheside (1942) in connection with chromosome break rejoining:

$$q(x) = 2x - 2x^2\left[1 - \exp\left(-\frac{1}{x}\right)\right] \qquad (2)$$

Human cell lines derived from normal tissue and malignant tumours were irradiated with acute and continuous irradiation at various dose rates to determine initial survival curve slopes, assess SLDR capability, and establish for each cell line the change in survival probability due to SLDR with different dose rates. Unfed plateau-phase cultures were used to minimise the effects of cell proliferation and delayed plating was used to allow complete potentially lethal damage repair (PLDR) following acute and low dose-rate irradiation.

## MATERIALS AND METHODS

The normal cell lines used were diploid fibroblasts derived from lung (CCD-18 Lu and HS88 Lu) and skin (AG 1522). The tumour lines were derived from two malignant melanomas (RPMI 7951 and SK-MEL 28), an

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*Supported by Grant CA-24232-08, National Cancer Institute, DHHS, and American Cancer Society Clinical Oncology Career Development Award (Dr Marchese).

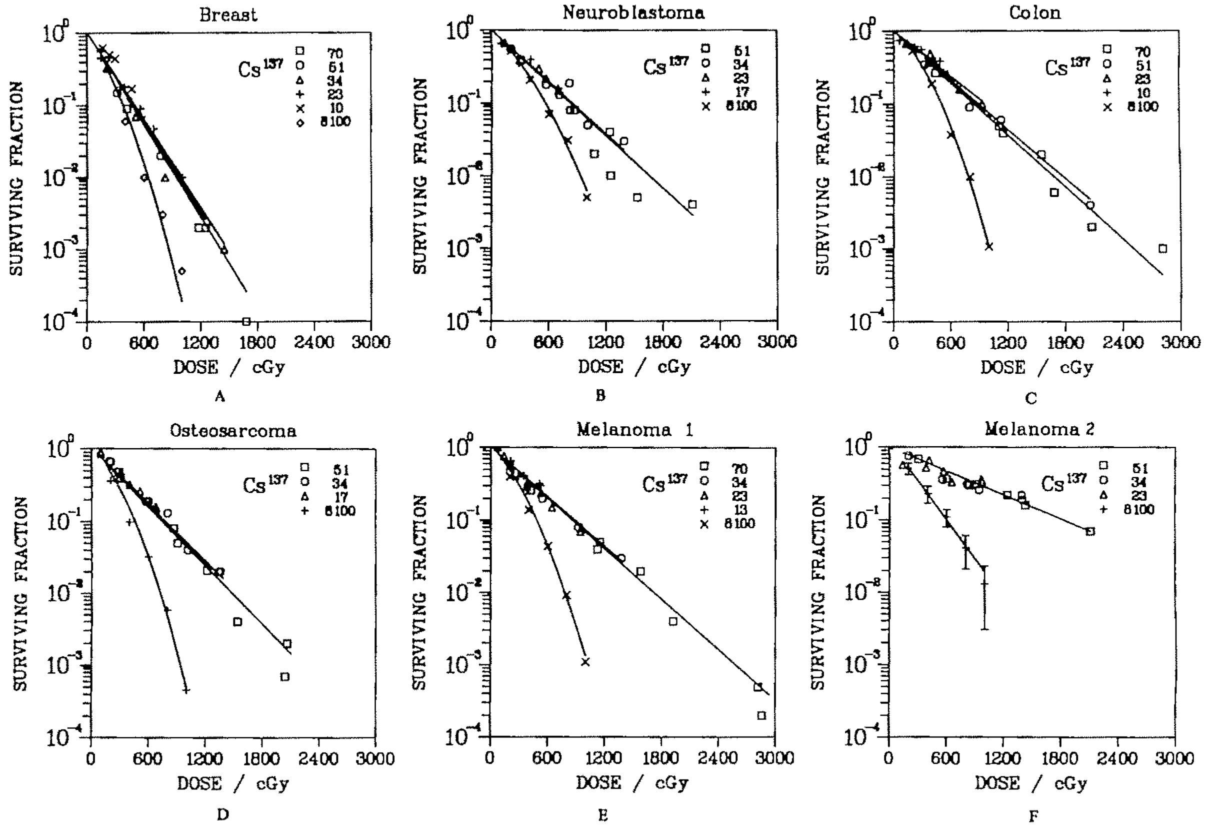

Fig. 1

Survival curves at dose rates of 10–8100 cGy/h for cells of malignant human tumour origin

osteosarcoma (U-20S), a colon carcinoma (SW-620), a breast carcinoma (MDA MB 231), and a neuroblastoma (SK-N-SH). 1–2 × $10^5$ cells were plated onto 35 mm petri dishes on Day 1. Cells became confluent on Day 4. Acute irradiation was performed on Day 8 and low dose-rate irradiation on Days 7–10. All irradiation was performed with $^{137}$Cs $\gamma$ rays. For acute exposures, the dose rate was 135 cGy/min while low dose-rate irradiation was carried out in a specially designed incubator containing $^{137}$Cs sources that yielded dose rates of 10–70 cGy/h. Cells were kept in 37°C, 5% $CO_2$ humidified incubators. McCoy's 5A or MEM media supplemented with 15% fetal calf serum, 50 $\mu$g/l gentamycin, 100 mg/l sodium pyruvate and 1 × non-essential amino acids was used. The medium was not changed until the cells were subcultured. Six hours after completion of irradiation the cells were trypsinised, counted, and replated onto 60 mm dishes so that 30–100 cells would survive to form colonies in each dish. The medium was changed every 5–7 days and colonies were stained and scored after 14–15 days. $5 \times 10^{-6}$ M bromodeoxyuridine was added to control dishes for a duration equivalent to the average cycle time at the time of irradiation. The percentage of positively staining cells (1000 counted/two dishes) from each experiment were averaged to obtain the percentage of cycling cells for each cell line.

## Results

Figures 1 and 2 show survival data for acute and various low dose-rate irradiations for six malignant and three normal fibroblast cell lines. Each point represents the weighted average of two experiments. As a general feature the data show little variation among the low dose rates, with a significant change only for the acute exposures (8100 cGy/h). It is clear then that SLDR processes must be quite fast, namely of the order of a fraction of an hour or less: only when doses were delivered within several minutes (as in the acute-exposure case) did a quadratic term, showing sublethal damage (SLD) *interaction*, become apparent. This is borne out by an analysis using Equation 1, the fits to the data of which are shown in the figures with solid lines. For each cell line the four or five sets of survival data were fitted together to three parameters: $\alpha$, $\beta$ and $t_0$. The results, shown in Table I, do indeed indicate that recovery constants, $t_0$, are short. It is instructive to note that $t_0$ is *not* the half-time for the $\beta D^2$ term: it

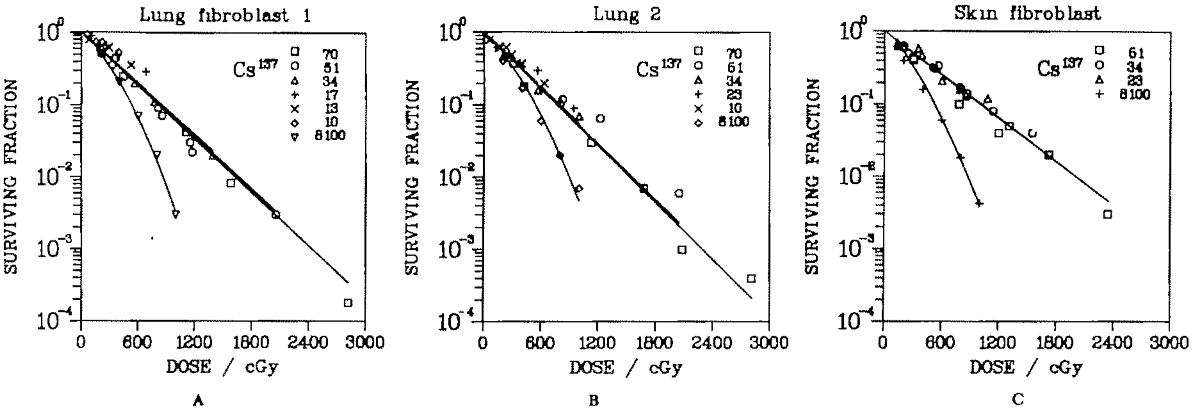

FIG. 2.

Survival curves at dose rates of 10–8100 cGy/h for normal human fibroblasts

takes an exposure time of about $3t_0$ to obtain 0.5 $\beta$ and even after $T = 10t_0$ a substantial fraction of the quadratic term (about 20%) remains. It is also apparent that the present experiments, while concentrating on dose rates of clinical significance, were not optimised in terms of obtaining values of $t_0$ (the gap between acute and the next dose rate is too large)

The malignant lines did not stop proliferating completely in the unfed confluent conditions. As shown in Table I, up to 32% of the cells were still cycling, as determined by BrdUrd-labelling of control dishes. Despite this, no significant differences in the cell survival curves over the 10–70 cGy/h range are demonstrated. Apparently, mitotic delay caused enough of an inverse dose-rate effect at the lowest dose rates to nullify the effects of proliferation for the 1–3 cell cycles of irradiation.

Table I also shows the values of $\alpha$ for the linear-quadratic fits to the data, as well as survival at 2 Gy for each cell line. Among the malignant lines, little correlation is seen between these parameters and clinical radiation response of the histological tumour types. The melanoma 2 line has a substantially smaller $\alpha$ (1.2) and higher $S$ at 2 Gy (0.79) than the other lines, while the breast carcinoma has a much steeper initial slope ($\alpha = 4\ 4$) and lower survival at 2 Gy (0.39) than the others. The seven other lines, however, fall into a narrow range of slope ($\alpha = 2\ 2$–2.8) and survival at 2 Gy ($S = 0.54$–0.64).

The SLD recovery ratios, defined as the ratios of survivals between acute and 70 cGy/h irradiation at the 1% survival levels, are also listed in Table I. The more resistant tumour types (2 melanoma, osteosarcoma and colon carcinoma) have recovery ratios of 13:1–24:1

TABLE I

SURVIVAL AND REPAIR PARAMETERS

| Cell line | Mean plating efficiency (%) | Mean % cycling | $S$ (2 Gy) | $\alpha \times 10^3$ cGy$^{-1}$ | $\beta \times 10^6$ cGy$^{-2}$ | $t_0$ (min) | SLD recovery ratio ($S = 0\ 01$) |
|---|---|---|---|---|---|---|---|
| Melanoma 1 (RPMI-7951) | 15 | 26 | 0.59 | 2 5±0 4 | 5.0±0 2 | 11 | 13:1 |
| Melanoma 2 (SK-MEL 28) | 8 | 19 | 0.79 | 1 2±0.2 | 23±10 | 1 | 24·1 |
| Osteosarcoma (U-20S) | 27 | 32 | 0.57 | 2.7±0 5 | 5.2±0.3 | 46 | 14:1 |
| Colon carcinoma (SW620) | 31 | 28 | 0 64 | 2 2±0 7 | 4.9±0 1 | 51 | 17 1 |
| Breast carcinoma (MDAMB 231) | 10 | 16 | 0.39 | 4.4±0.1 | 4 3±0.4 | 50 | 6.1 |
| Neuroblastoma (SK-N-SH) | 25 | 29 | 0 58 | 2 6±0 1 | 2 6±0 2 | 35 | 8·1 |
| Skin fibroblast (AG 1522) | 18 | 5 | 0 62 | 2 2±0.1 | 5.4±0 3 | 4 | 14:1 |
| Lung fibroblast 1 (CCD-18 Lu) | 8 | 3 | 0 60 | 2 5±0 8 | 3.4±0 1 | 43 | 11·1 |
| Lung fibroblast 2 (Hs 88 Lu) | 24 | 5 | 0 54 | 2 8±0 9 | 2 7±0.2 | 27 | 7·1 |

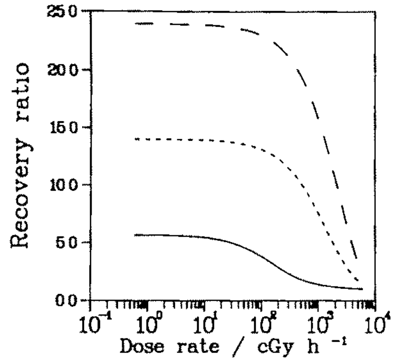

Fig 3

Sublethal damage recovery ratios at various dose rates (survival compared with 8100 cGy/h at 1% survival level) for —— breast, - - - - skin fibroblast and — — — melanoma 2 cell lines

while the breast and neuroblastoma tumour cell lines have lower recovery ratios (6 : 1 and 8 : 1). The normal fibroblast lines demonstrate a repair capacity intermediate between the two malignant groups (7–14 : 1).

## Discussion

Several points can be made from this study. In this small group of malignant cell lines, there is no correlation between clinical resistance of tumour cell types and either initial slope ($\alpha$) or survival at 2 Gy. This differs from the results of two other studies (Brock et al, 1986; Malaise et al, 1986), but is not surprising. In the large group of cell lines studied by Malaise et al (1986) there was a large amount of overlap among the tumour types and large variation in coefficients. Also, the oat-cell carcinoma group appeared considerably more sensitive *in vitro* than the non-small-cell carcinoma and even the lymphoma groups. This is clearly not representative of the clinical experience (Choi & Carey, 1976, Mira & Livingston, 1980). The preliminary results of fresh explants by Brock et al (1986) also tend to show some correlation with tumour type on the basis of 2 Gy doses, but again there is considerable overlap.

Another factor may be that the cell lines in this study were well established *in vitro*, which may tend to make radiation responses more similar than in the original tumours. It would be of interest to test the correlative value of continuous irradiation on fresh tumour explants. In addition to more precise estimation of the initial survival slope, the protracted irradiation also evaluates the extent of SLDR and PLDR capacities of the cells, which are important aspects of clinical response. At 70 cGy/h, irradiation time is limited to less than one cell cycle so that proliferation does not significantly affect survival.

Another conclusion of this study is that SLDR is significant in all the cell lines and is, on average, of larger magnitude than the corresponding PLDR (Marchese et al, 1986) This is particularly true of the four more clinically resistant tumour types which showed large SLD recovery ratios (13 : 1–24 : 1) and small PLDR ratios (<3 : 1). The normal fibroblasts showed substantial SLDR and PLDR, although SLDR was more important (SLDR recovery ratios of 7–14 . 1 vs 4–6 : 1 for PLDR). Such information will be useful in deciding which tumours to include in repair inhibitor protocols and, more immediately, in hyperfractionation protocols. Tumours with large SLDR capability would not be good candidates for hyperfractionation or brachytherapy studies.

Finally, the data show that SLD repairs relatively rapidly in human cells, so that dose rates of 10–70 cGy/h are essentially equivalent in terms of cell killing This is further illustrated in Fig. 3 for three cell lines (breast, skin fibroblast and melanoma). The recovery ratio, defined above, changes significantly with dose rate only above 100 cGy/h. The extent of this change is roughly inversely proportional to the recovery constant, $t_0$. Our dose-rate findings are in agreement with clinical data reported by Pierquin (1976), who found dose rates of 25–100 cGy/h to give similar results. Cell proliferation, however, may become an important factor in permanent implants. Higher dose rates should be investigated further, particularly since they are becoming popular in remote-afterloading implants

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# The effect of ethanol on the radiation response of CHO-K1 cells

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(*Received September 1986 and in revised form November 1986*)

ABSTRACT

The radiobiological response of CHO-K1 cells treated with ethanol is described. Both radioprotective and radiosensitising effects were found, depending on the duration of exposure before irradiation and the number of cells exposed. In spite of effects of ethanol on the shoulder of the primary survival curve, split-dose recovery was not affected. The radiobiological effect of alcohols is normally attributed either to radical scavenging or to oxidation. The findings presented here do not support either of these mechanisms.

Ethanol is known to have a small radioprotective effect. This has been demonstrated in mice (Paterson & Matthews, 1951), bacteria (Hollaender & Stapleton, 1953), plant bulbs and seeds (Riley, 1955) and protozoa (Kimball & Gautier, 1951). The effect is normally observed only after prolonged exposure or exposure to high concentrations (~ 0.7 M) and is thought to involve either radical scavenging by the hydroxyl group of the ethanol molecule, or depletion of cellular $O_2$ levels by metabolic oxidation of ethanol to acetaldehyde (Hollaender, 1960).

Recently, while ethanol was being used as a solvent during a study of the radioprotective effect of vitamin A over a 24 h period before irradiation (Mothersill et al, 1987), both a transitory radioprotective effect and a pronounced sensitising effect due to ethanol alone, which could be induced under different culture conditions, were noted. These effects suggest an alternative mechanism of action which cannot easily be explained by the above hypotheses.

## METHODS

### Cell culture

The cell culture system and methods of irradiation are described in detail elsewhere (Seymour & Mothersill, 1981). Briefly, CHO-K1 cells (Flow Laboratories) were maintained in Ham F-12 medium supplemented with 10% fetal calf serum, 25 mM Hepes (Gibco) and 4 IU gentamicin sulphate. Cells were subcultured using trypsin (0.25%) and versene (1 mM) in a 1 : 1 ratio for detachment.

For the experiments, two procedures were followed.

(a) The cells were plated 4 days before irradiation and after 3 days, when cultures were confluent, the medium was changed. At selected time intervals during the remaining 24 h ethanol was introduced to the cultures in 0.5 ml medium to give a final concentration of 1.57 M. Using this concentration, plating efficiencies of control and ethanol-treated cells were not significantly different. Controls were given 0.5 ml medium only. Three hours after irradiation the cells were trypsinised, diluted and plated at cloning densities. Survival was assessed using the technique of Puck and Marcus (1956), which involves counting the macroscopic colonies (~ 200 cells) formed after 7 days.

(b) The cells were plated at cloning densities (100–10 000 cells) 24 h before irradiation. The ethanol and medium were introduced as described above and removed by a change of medium 3 h after irradiation. Seven days after irradiation, survival was assessed as described above.

### Assay of ethanol and alcohol dehydrogenase

Ethanol concentrations in medium were determined using the Boehringer Corporation Limited blood alcohol test combination No. 123960. The principle of the test involves the conversion of ethanol to acetaldehyde with the formation of reduced nicotinamide adenine dinucleotide (NAD). This was measured at 340 nm using a Clinicon spectrophotometer. Alcohol dehydrogenase (ADH) activity was measured using p-nitroso-dimethylalanine in the recycling assay of Dunn & Bernhard (1971).

## RESULTS

Addition of 1.57 M ethanol to confluent cultures of CHO-K1 cells at selected time intervals produced a transitory radioprotective effect, which was greatest when the addition took place 3–6 h before irradiation and fell off when the addition took place less than 3 h or more than 9 h before (Fig. 1). The addition of ordinary medium had a similar but smaller effect.

Survival curves (Fig. 2) for similar confluent cultures of CHO-K1 cells given either ethanol or ordinary medium 24 h or 5 h before irradiation indicated that, after treatment, the $D_0$ increased from 2.0 Gy for both 24 h curves to 2.4 Gy for the control 5 h curve and 2.9 Gy for the ethanol 5 h curve.

When 1.57 M ethanol or medium only was added to

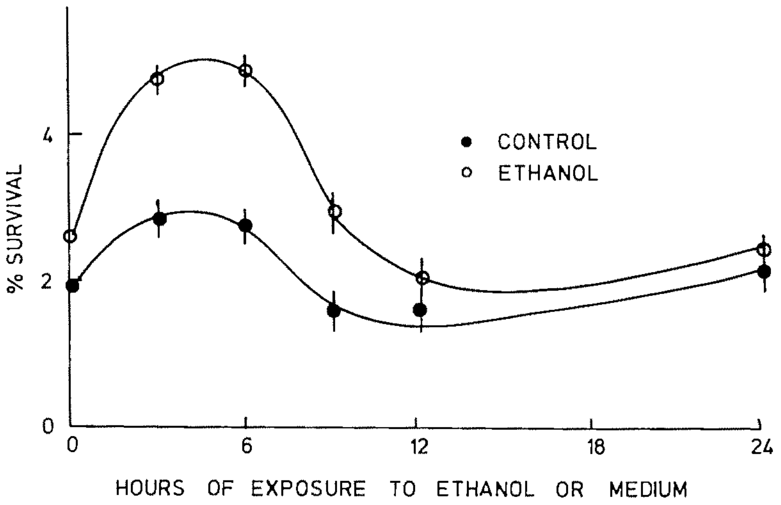

FIG 1.

Effect of addition of 1.57 M ethanol or ordinary medium at various times before irradiation (10 Gy) on the % survival of CHO-K1 cells

cultures seeded at cloning densities, ethanol was found to reduce the relative survival of cells when added 18 h or 6 h before irradiation (Fig. 3), whereas addition of medium 6 h before irradiation produced a smaller radioprotective effect. Addition of medium 18 h before had no effect.

A lower concentration of ethanol (78 mM) added to cloning densities of cells resulted in a smaller radiosensitising effect (Fig. 4). When cloning densities of cells were exposed to 1.57 M ethanol for 18 h before a fractionated dose of radiation (Fig 5) there was no inhibition of split-dose recovery in spite of a significant reduction in the size of the shoulders of the primary curves.

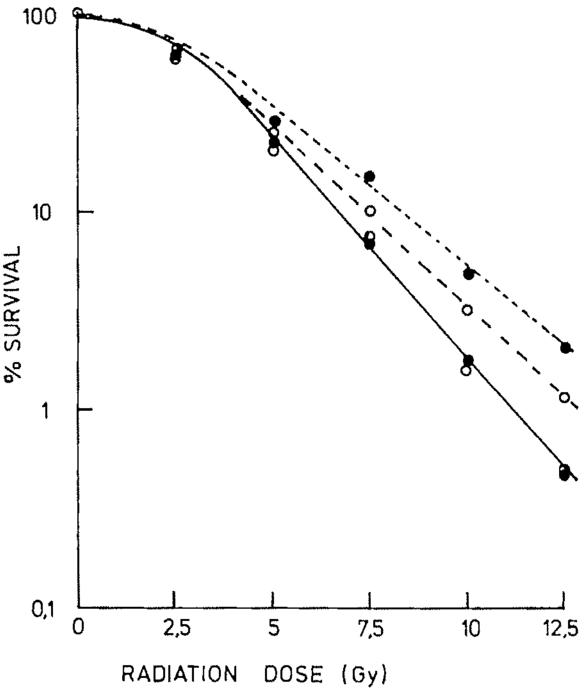

FIG 2.

Radiation survival curves for dense cultures of CHO-K1 cells exposed to 1.57 M ethanol (●) or ordinary medium (○) for 24 h (——) or 5 h (– – – – –) before irradiation

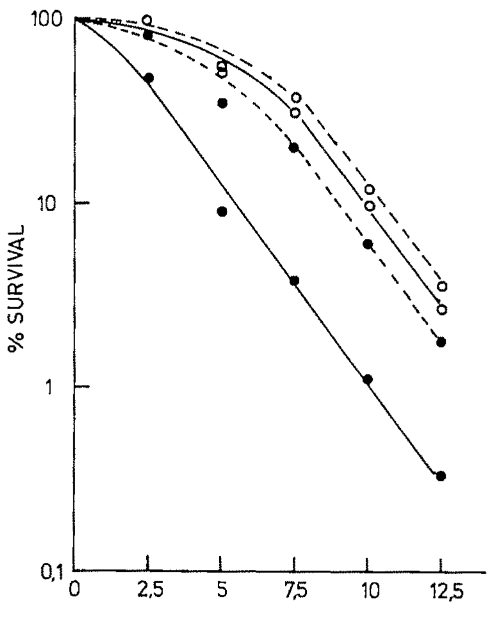

FIG. 3

Radiation survival curves for two to four cell microcolonies of CHO-K1 cells exposed to 1.57 M ethanol (●) or ordinary medium (○) for 18 h (——) or 3 h (– – – – –) before irradiation

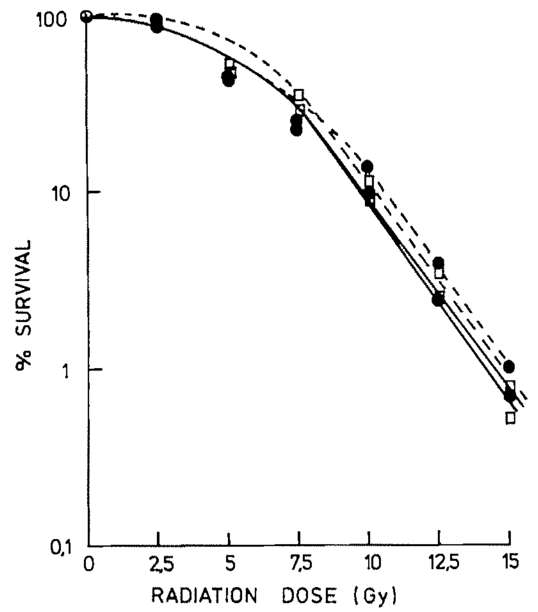

FIG. 4.

Comparison of the effects of exposure to low (78 mM, ●) concentrations of ethanol for 18 h (——) or 3 h (– – – – – –) on the radiation survival curve of CHO-K1 microcolonies (controls, □– – – –□)

In an attempt to interpret these results—in particular the reason for the cell-density dependence of the effect and the mechanism(s) by which ethanol is acting—the following experiments were designed.

*Breakdown of ethanol by CHO-K1 cells*

Table I shows the levels of ethanol detected in 5 ml medium from confluent cultures (4 x $10^6$ cells) to which ethanol had been added over a 24 h period. It is clear that no significant breakdown of ethanol takes place. This was confirmed by assay of the ADH level, which showed that the activity of the enzyme was only 0.19 nmol/min/mg protein. This should be compared with an activity of 1.08 μmol/min/mg protein for lactate dehydrogenase. These results would appear to preclude the possibility that ethanol was significantly affecting the cellular redox state. Although these results do not rule out a possible involvement of the microsomal ethanol oxidation system (Ohnishi & Lieber, 1977) or catalase (Lieber, 1977), the data in Table I suggest that such a contribution must be relatively small.

TABLE I

ETHANOL LEVELS DETECTED IN MEDIUM SAMPLES FROM CONFLUENT CELLS EXPOSED FOR 0–24 H TO 1.57 M ETHANOL BEFORE IRRADIATION (10 GY)

| Exposure time to ethanol | % of added ethanol detected at the time of irradiation |
|---|---|
| Control (no ethanol) | – |
| 24 h | 95.0 ± 10.5 |
| 12 h | 97.5 ± 5.1 |
| 9 h | 95.0 ± 7.9 |
| 6 h | 90.0 ± 8.3 |
| 3 h | 100.0 ± 5.0 |
| 0.5 h | 95.0 ± 10.5 |
| 0 h | 100.0 ± 7.5 |

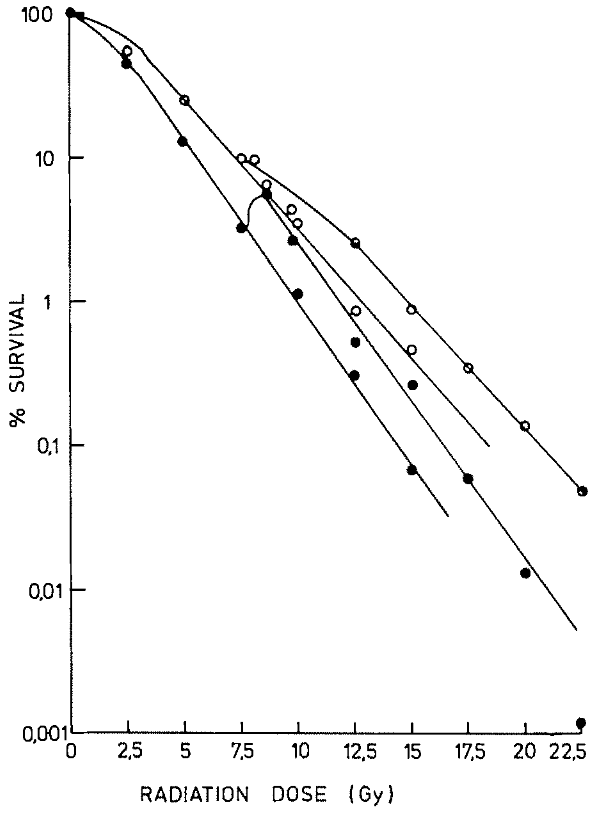

FIG. 5

Primary and secondary survival curves for CHO-K1 microcolonies given their first dose of irradiation 18 h (——) after exposure to 1.57 M ethanol (●) or ordinary medium (○).

*Investigation of the effect of addition of medium to cultures before irradiation*

Addition of medium to confluent cultures serving as controls in the radiation experiments revealed a radioprotective effect which was similar to, though smaller than, that observed following ethanol addition. Table II and Fig. 6 show results of experiments where flasks received a complete or partial medium change or were merely briefly opened 5 h before irradiation. It is clear that all these treatments raise the level of survival (Table II) and the survival curves shown in Fig. 6 confirm this.

TABLE II

The effect of agitation, exposure to air and the addition of medium 5 h before incubation on the survival of confluent cultures of CHO-K1 cells exposed to 10 Gy*

| Treatment | % survival | Significance |
|---|---|---|
| No treatment | 1.08±0.08 | – |
| Flask agitated for 2 min | 1.39±0.11 | NS |
| Flask opened for 4 min | 2.32±0.24 | $p < 0.05$ |
| Flask opened, +0.5 ml fresh medium introduced | 3.08±0.06 | $p < 0.001$ |
| Flask opened and complete fresh medium change given | 8.96±0.92 | $p < 0.001$ |

*Experimental details are given in the text Results are expressed as mean ± standard error for six experimental points

### *Effect of tertiary butanol*

Table III shows the results of experiments designed to test the effect of a metabolically inert alcohol. It is apparent that tertiary butanol had no effect on the radiation response, except at levels where it was highly toxic.

## Discussion

Alcohols are well known radioprotective agents (see Bacq and Alexander (1961) for review) but their action in the cell has usually been attributed to their radical-scavenging abilities or to cellular $O_2$ depletion by oxidation of ethanol to acetaldehyde. Two effects are reported here, however, and neither can easily be explained on the basis of the above mechanisms.

The first effect is a transitory radioprotective effect resulting in an increase in the $D_0$ of the survival curve, detected only when confluent cultures of CHO-K1 cells have been exposed to ethanol for 3–6 h before irradiation; longer or shorter times lead to cell-survival rates which are not significantly different from the controls.

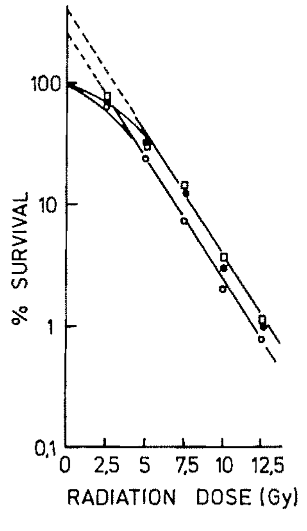

Fig 6

Radiation survival curves for CHO-K1 cells maintained in sealed flasks which were unopened (○), opened for 5 min (●) or received a complete medium change (□) 5 h before irradiation.

TABLE III

The effect of tertiary butanol on the radiation response of CHO-K1 cells (18 h exposure before 7.5 Gy)

| mM tertiary butanol | % survival | | Significance |
|---|---|---|---|
| | Control | Irradiated | |
| 0 | 100.0 ±8.8 | 13.2 ±1.16 | |
| 4.0 | 98.9 ±0.28 | 16.9 ±0.91 | NS |
| 20.0 | 94.4 ±2.9 | 14.5 ±0.55 | NS |
| 400.0 | 0.28±0.28 | 0.141±0.075 | $p < 0.001$ |

The mechanism for this transitory radioprotective effect may relate to the introduction of oxygen or small amounts of medium into the flask since a small level of protection was afforded by adding 0.5 ml of medium to confluent flasks 3–6 h before irradiation. The experiment comparing the effects of merely opening flasks, adding or changing medium 5 h before irradiation would seem to confirm this.

This could suggest a mechanism involving increased energy production before irradiation resulting from the introduction of oxygen and energy substrates into the flask, since these substances are known to stimulate cellular recovery from radiation damage (Kiefer, 1971; Nishizawa et al, 1979). Attempts to show that ethanol might be being used as an energy substrate, however, failed, since no detectable breakdown of the alcohol occurred and assays for ADH activity in the cell revealed only very low activity. The alcohol may be having some influence on metabolism, however, because the metabolically inert alcohol tertiary butanol had no protective effect and was inactive except at levels where it was toxic to cells

Further evidence for a mechanism involving alleviation of cellular hypoxia is given by the data showing no protection whatever (indeed, showing significant radiosensitisation) when ethanol was introduced to single cells or microcolonies set up 6–18 h previously. In this case there should be no medium depletion and oxygen levels in the medium and flask would be high.

Relief from hypoxia before irradiation is known to affect the cells' ability to repair radiation damage (Malone & Foster, 1972) and Seymour and Mothersill (1981) have shown that addition of lactate to cells for short periods before irradiation can induce a small degree of radioprotection. The latter authors have also shown that lactate can increase recovery levels between split doses of irradiation (Mothersill et al, 1987). Since ethanol and lactate are both potential sources of reducing equivalents and energy metabolites in the cell, it is tempting to suggest that the radioprotective effect involves similar mechanisms to those resulting from the administration of other energy substrates. However, in the case of ethanol its metabolic effects must involve enzyme systems other than ADH.

The second radiobiological effect found was a sensitising of cells exposed to high levels of ethanol. This occurred only when very low cell numbers were treated and was accompanied by significant toxicity of unirradiated controls. It is in some ways similar to the effect of high vitamin A levels (Mothersill et al, 1987) and could relate to membrane lysis which would be aggravated by radiation exposure (Medvedev et al, 1977; Alper, 1979) and could be expected to be most severe where few cells were available to take up the ethanol. It is interesting, however, that although the effect is associated with a significant reduction in the extrapolation number of the survival curve, reduction in split-dose recovery, which is conventionally thought to be associated with a reduced *n*, does not appear to occur. This type of radiation response is also found with lactate and glucose analogues and glycolysis inhibitors (Seymour & Mothersill, 1981; Seymour et al, 1985; Mothersill & Seymour, 1986; Seymour & Mothersill, 1987) and further strengthens evidence that a mechanism involving glycolytic energy metabolism is involved in the radiation response of cells pre-treated with ethanol.

## ACKNOWLEDGMENTS

The support for this work is provided by the EEC Radiation Protection Programme (Contract No. B16-092-IRL) and the Irish Cancer Research Advancement Board and is gratefully acknowledged.

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# Book reviews

*Physician's Guide to Cancer Care Complications. Prevention and Management. Fundamentals of Cancer Management* Vol. 2. Ed by John Laszlo, pp. xii+360, 1986 (Marcel Dekker, New York), $71.50.
ISBN 0–8247–7547–3

As cancer survival stagnates, attention has recently been focused on quality of life and management. This book is a timely, constructive and comprehensive attempt to address these issues and, in general, succeeds in its aim.

Cancer patients experience a very wide spectrum of problems; some of these are not usually regarded as within the province of the medical team, others may be caused or aggravated by inappropriate management Early on, a chapter tackles the economic hardships suffered by the patient and family; although written in an American context, the arguments for common sense, efficiency, cost control and realism are widely applicable. This chapter also emphasises the emerging truth that our ability to diagnose is far outstripping our ability to cure and encourages reflection rather than reflexes when ordering investigations. Potential areas of conflict (for example between research and economy) are not avoided in this or other chapters.

An important theme throughout the book is that of a therapeutic relationship. To the extent that this subject lends itself to a didactic approach, the book succeeds in analysing its components, its founding and the direct and indirect benefits which flow from it Detailed sections follow on the application of this principle to the traditional areas of doctor-patient contact in oncology

The chapter on chemotherapy complications is valuable and exhaustive, dealing not only with the well known organ toxicities but also with such relatively neglected but symptomatically vital areas as venous access There is also a useful section guiding personnel who handle cytotoxics

The chapter on surgery legitimately draws attention to background fluid, electrolyte, nutritional and haematological problems, but goes into far too much unnecessary physiological detail By contrast there is little discussion on the appropriateness of various operative procedures, the tone of the book would reasonably demand at least some reference to the mastectomy debate, for instance.

The anticipation and management of radiotherapy complications is well set out although, curiously, there is no mention of hypothyroidism until the chapter devoted to paediatric problems Central nervous system complications merit an entire chapter, as does the important topic of psychiatric morbidity in the cancer patient. Much of this is treatable, the clinical point about antidepressants potentiating other methods of pain control is well made.

The chapter on the special problems of the elderly is almost spoiled by jargon, readers on this side of the Atlantic will surely find such phrases as "biopsychosocial profile" unnatural, pompous and off-putting

The last two chapters on support services for hospitalised patients and the care of the dying are particularly full of insight and sensitive

Few illustrations or diagrams are required and in general the book does not waste space on them References, by and large, do not postdate 1984 but this in no way detracts from the book and I commend it to all who are involved in the care of cancer patients. At just under £50.00 it is not cheap, but serious oncologists would do well to add it to their libraries

M VINCENT

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*Radiotherapy in Clinical Practice* Ed. by H. F. Hope-Stone, pp 454, 1986 (Butterworth Group, Sevenoaks), £45 00.
ISBN 0–407–00430–7

The editor states in the preface that the book is meant to be a source of information for experienced and trainee radiotherapists To that end, radiotherapeutic techniques are described in detail but no attempt is made to cover surgery and chemotherapy in similar detail There are 20 chapters, written by 15 authors, 10 of whom are based at centres in London.

The opening chapter, very sensibly, deals with radiobiology. The extensive data available on the subject are clearly summarised from a clinical point of view, showing the relevance to dosage, fractionation and the effects of irradiation. There is an overlap with the next chapter on radiosensitisers, which describes briefly the basis of radiosensitisers and the clinical work done up to the present

The treatment of neoplasms of the bladder is dealt with in great detail based on the author's extensive experience. Staging, techniques, morbidity, results and a review of other series are all discussed clearly. In contrast, very little is said about testicular teratomas, and one has to turn to Chapter 20 to get the chemotherapeutic details of treatment.

The chapter on breast cancer is in fact a very extensive review of the world literature from Halstead (1907) to Veronesi (1985), on the treatment of operable breast cancer. The next three chapters on head and neck cancer, soft-tissue sarcomas and intrathoracic tumours are all of a high standard, clearly written and with a lot of practical information

In the chapter on lymphomas, the author does admit that radiotherapy cannot be considered in isolation from chemotherapy, and this makes for easier reading A lot of the work is based on previously reported BNLI studies, and due acknowledgment is given to the collaborators at the end of the chapter The treatment of gynaecological malignancies is based entirely on techniques used at the Christie Hospital in Manchester Other chapters deal with the treatment of malignancy in children, skin, gastrointestinal, central nervous system, endocrine and haematological systems. The latter covers the techniques for bone marrow transplantation.

The presently fashionable interstitial implant techniques with iridium 192 are also described. An unusual contribution is the chapter on the treatment of benign conditions with radiotherapy. The book ends with chapters by a radiographer, a physicist and a medical oncologist giving their viewpoints on the treatment of malignancies.

As a textbook it is full of practical information, is easy to read and the illustrations are excellent The references are very extensive and right up to date. The price is reasonable and I would have no hesitation in recommending its purchase both by libraries and by individual radiotherapists

G. G. RIBEIRO

1987, *The British Journal of Radiology*, *60*, 583–588 JUNE 1987

# The effect of mixed fractionation with X rays and neutrons on tumour growth delay and skin reactions in mice

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(*Received December 1986 and in revised form January 1987*)

ABSTRACT

We have compared the effects of mixed fractionation schedules with X rays and neutrons on growth delay of a murine tumour and skin reactions in mice The schedules were five daily fractions of X rays, neutrons or mixtures (NNXXX, XXXNN or NXXXN). For clamped tumours or skin all three mixed schedules had the same effect. In contrast, for unclamped tumours giving the neutrons first (NNXXX) was more effective than the other two mixed schedules This represented a true therapeutic gain and implies that if neutrons are used clinically as only part of a course of fractionated radiotherapy, they should be given at the beginning rather than at the end of treatment

There are many possible reasons why clinical radiotherapy may fail to cure patients of their primary tumours. The inability to kill a sufficient number of tumour cells without causing unacceptable normal tissue damage might reflect differences in intrinsic radiosensitivity. or in capacity to repair radiation damage, or may be due to the presence of clonogenic hypoxic cells in tumours. One approach to overcoming these problems is to use a high-LET radiation, such as neutrons. Factors which modify the radiation response of cells are generally less effective with high- than with low-LET radiation (see Fowler, 1983). Neutrons may also be of benefit if the reduction in dose per fraction "wasted" in inflicting sublethal damage were greater for tumours than for normal tissues (Alper, 1972; Howlett et al, 1975). A further potential advantage of neutrons may stem from the reduced radioresistance of cells in S-phase and in long G1 phase to neutrons relative to X rays, as might be the case in slowly proliferating human tumours (Withers & Peters, 1980; Fowler, 1983).

A number of Phase I and Phase II clinical trials have used neutrons in a mixed-fractionation scheme in which two doses of neutrons and three doses of $\gamma$ rays were given each week (*e.g.* Griffin & Laramore, 1982; Duncan et al, 1986). Such schedules may have practical advantages in circumstances where there may be limited access to a neutron source. In at least one Phase II trial there was evidence that mixed fractionation might be more effective than a fractionation scheme consisting of neutrons or photons alone (Griffin & Laramore, 1982). There is some experimental evidence to support this observation. Rasey et al (1977) found that two fractions of neutrons followed by three fractions of X rays had a higher therapeutic gain factor when treating EMT-6 tumours in mice than five fractions of neutrons. The authors offered various explanations for this result, but presented no evidence in favour of any of them.

If neutrons achieve their benefit through greater killing of hypoxic cells, then one might expect that, in a mixed-fractionation scheme, giving the neutrons at the start of treatment would be more effective than giving them at the end (Denekamp et al, 1978). We have addressed the question of whether mixed fractionation produces a greater therapeutic gain than neutrons alone and have investigated whether or not this gain results from the increased effectiveness of neutrons against hypoxic cells. We have measured tumour growth delay using a transplanted mouse tumour and skin reactions in mouse feet, using the same fractionation schedules to estimate potential therapeutic gain (*i.e.* the increase in tumour effect in changing from X rays or neutrons alone to a mixed-fractionation schedule, when the normal tissue effect is kept constant).

## MATERIALS AND METHODS

### *Tumour experiments*

A syngeneic transplantable sarcoma (SaF) was transplanted on to the backs of CBA/Ht/fGyBSVS male mice aged 16 weeks. Tumours were irradiated when they had reached a geometric mean diameter of about 6 mm. The methods for transplanting were as previously described (McNally et al, 1979). Tumours were irradiated in unanaesthetised mice breathing air, with 240 kVp X rays or neutrons as described before (McNally et al, 1982). In one series of experiments, clamps were applied to the tumours to occlude the blood supply 10 min before irradiation.

Tumour regrowth time was determined by plotting the geometric mean tumour diameter against time for each mouse and determining the time to increase in diameter by 3.5 mm from the size at the start of treatment (a roughly fourfold increase in volume). The mean regrowth time and its standard error were calculated for each dose group consisting of six to eight mice. A mean growth delay was then calculated by taking the difference between this value and that for unirradiated mice.

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TABLE I

DOSES (IN GY) GIVEN TO UNCLAMPED TUMOURS

| Single doses | | Five fractions | | Mixed fractionation |
|---|---|---|---|---|
| X rays | Neutrons | X rays | Neutrons | |
| 5 | 2 | 10 | 3.75 | $2\times0.75N+3\times3X$ |
| 10 | 5 | 20 | 6.25 | $2\times1.25N+3\times5X$ |
| 15 | 10 | 25 | 8.75 | $2\times1.75N+3\times7X$ |
| 25 | | 35 | 12.25 | $2\times2.5N+3\times9X$ |
| 35 | | | | |

TABLE II

DOSES (IN GY) GIVEN TO MOUSE SKIN

| Five fractions | | Mixed fractionation |
|---|---|---|
| X rays | Neutrons | |
| 35 | 8.85 | $2\times1.75N+3\times7X$ |
| 40 | 10.7 | $2\times2.15N+3\times8X$ |
| 45 | 12.6 | $2\times2.7N+3\times9X$ |
| 50 | 14.65 | $2\times2.95N+3\times10X$ |

Irradiation was with either single doses of X rays or neutrons, or five doses 24 h apart. These were either all X rays, all neutrons or two doses of neutrons plus three doses of X rays. In this case, the neutrons were given at the beginning (NNXXX) or the end (XXXNN) or one dose at the beginning and one at the end (NXXXN)

The doses for fractionated irradiation were chosen using previous data for single doses of neutrons or X rays (McNally et al, 1982). Each dose of X rays or neutrons in the mixed schedules was chosen to be isoeffective on the basis of single-dose data, so that each complete schedule (NNXXX, XXXNN, NXXXN) would, on this basis, have the same overall effect. The doses chosen are listed in Table I. For the more limited study with clamped tumours, only the mixed schedules were used at two total dose levels of 47 Gy and 64.5 Gy, using assumed oxygen enhancement ratios of 2.8 and 1.7 for X rays and neutrons respectively to calculate the appropriate doses.

### *Skin experiments*

For skin-reaction measurements, adult male albino mice (WHT/GyfBSVS) aged 14–16 weeks were used, with four mice in each treatment group. Animals were irradiated unanaesthetised in air, according to the methods of Douglas and Fowler (1976). Briefly, mice were restrained in lead boxes from which the left hind foot protruded, which was held gently in position within the irradiation field by three perspex posts. Irradiation was carried out using 240 kVp X rays at a dose rate of 2 Gy $\text{min}^{-1}$, or neutrons at a mean dose rate of 0.6 Gy $\text{min}^{-1}$. These irradiation procedures for mouse feet have been described in detail by Joiner et al (1986).

Skin reactions were scored three times a week from 7 to 35 days post-irradiation, using the ordinal scale of Fowler et al (1965) as implemented by Douglas and Fowler (1976) and Joiner et al (1986). For each mouse, the scores for each day within a specified period (usually 10–32 days) were added together and the result divided by the number of days, giving an "average" daily score. These values were then averaged for all the mice in a dose group to give a mean average skin reaction. Since the scoring scale is ordinal, these procedures have no strict statistical validity (Denekamp et al, 1984), but they enable smooth monotonic dose–response curves to be constructed. This allows a direct comparison of the effectiveness of the different mixed-beam schedules by comparing isoeffective doses.

The irradiation schedules were identical to those chosen for the tumour experiment (5F "N", 5F "X", NNXXX, XXXNN, NXXXN). Each dose of neutrons or X rays in each schedule was chosen to be isoeffective with each complete schedule also having the same effect overall. This was achieved by using previously published data on the relative effectiveness of neutrons and X rays in mouse skin (Joiner et al, 1983, 1984) Table II shows the doses used

## RESULTS

Figure 1 shows growth delay curves for tumours exposed to single doses of X rays or neutrons. These are very similar to data published previously (McNally et al, 1982) The error bars represent standard errors of the mean for six to eight mice per dose group. Figure 2 shows the growth delay curves for unclamped tumours exposed to five fractions of X rays, or neutrons, or the mixed-fractionation schedules. Five fractions of X rays was least effective for a given total dose and five fractions of neutrons the most effective. The mixed-fractionation schedules giving the neutrons at the

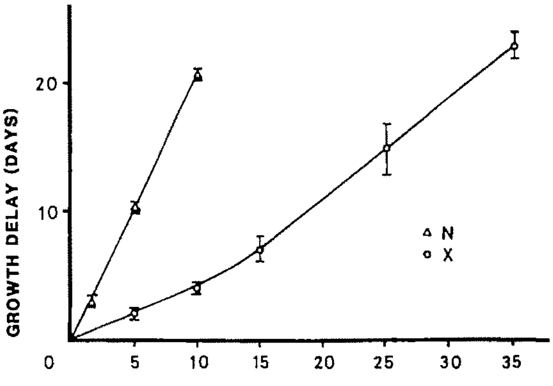

FIG. 1

Tumour growth delay after single doses of X rays (○) or neutrons (△). (Error bars in this and subsequent figures are 1 SEM)

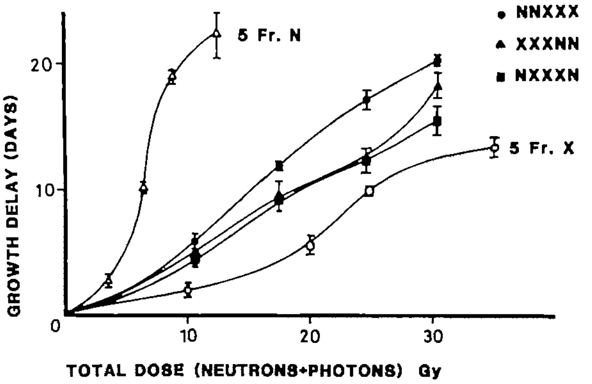

Fig. 2.

Tumour growth delay after five daily fractions of X rays (○), neutrons (△) or mixed schedules.

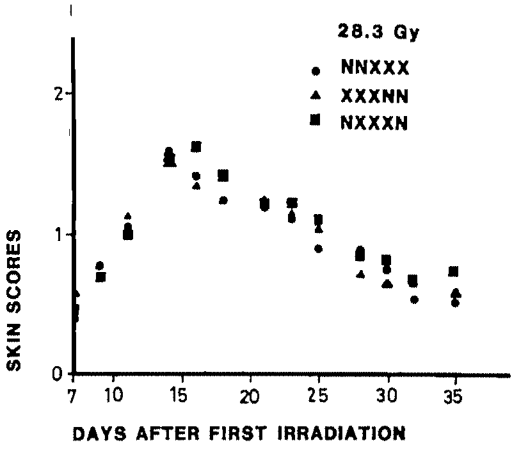

Fig. 4.

Skin reaction as a function of time for the three mixed-fractionation schedules, for a total dose of 28 3 Gy.

beginning and end (NXXXN) or at the end (XXXNN) gave essentially identical curves. In contrast, giving them at the beginning (NNXXX) was more effective over the whole dose range, although the difference was not significant at the lowest total dose used. For growth delays in the range 5–15 days, giving the neutron doses at the beginning and end, or at the end, meant increasing the total dose by a factor of about 1.24 relative to giving the neutron doses at the beginning.

In order to determine whether this result could represent a true therapeutic gain for giving the neutrons first, acute skin reactions in the mouse foot were used as a model normal tissue, for identical fractionation schedules. The average skin reaction, determined as described in the previous section, was plotted as a function of the total dose (Fig. 3). Five fractions of neutrons alone was the most effective schedule and five fractions of X rays the least effective, as would be expected from simple considerations of fractionation effects in the absence of hypoxia. The dose–effect curves for the three mixed-fractionation schedules were essentially identical, in contrast to the tumour results (Fig. 2). This is also shown in Fig. 4, where the skin reactions have been plotted as a function of time after irradiation for each of the three mixed schedules for a total dose of 28.3 Gy. The rise in skin reaction, the peak reaction and the recovery are the same for each schedule both in magnitude and in their temporal relationship to the time of irradiation.

In tumours, reoxygenation of hypoxic cells can increase their sensitivity to a subsequent dose, and may even more than counteract recovery from sublethal damage (Denekamp & Harris, 1976). In skin, hypoxic cells are much less likely to influence the response to fractionation (Stewart et al, 1982). In order to investigate the consequences of eliminating the mixed oxic and hypoxic cell population in tumours, a further limited experiment was performed in which tumours were clamped prior to each dose, using only the mixed-fractionation schedules. The doses were chosen as described in the previous section. However, because of dosimetry problems with an X-ray machine during the NNXXX schedule, the X-ray doses were 5% less than

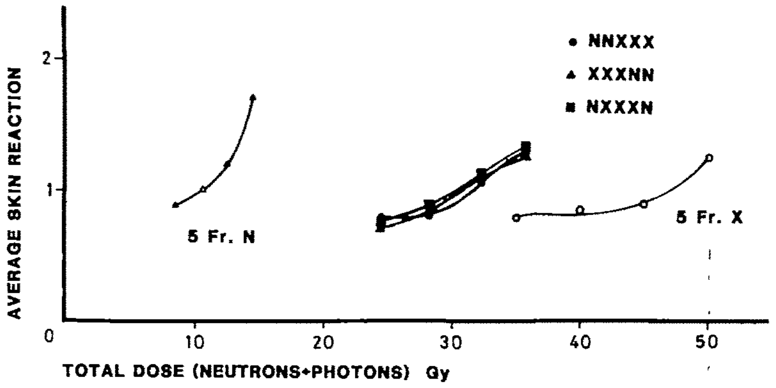

Fig. 3

Average skin reaction in mouse feet as a function of total dose for five daily fractions of X rays (○), neutrons (△) or mixed schedules.

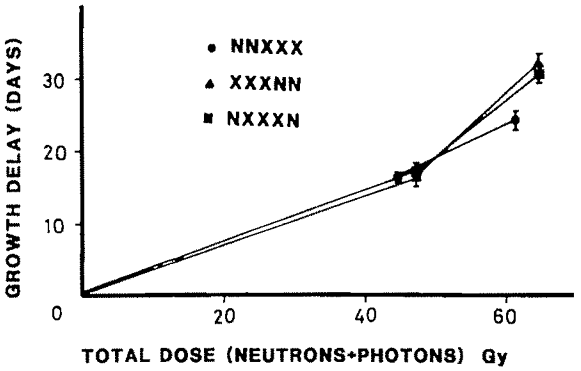

Fig 5

Tumour growth delay for tumours clamped prior to irradiation with the mixed-fractionation schedules

for the other two schedules, giving total doses of 44.9 Gy and 61.57 Gy instead of 47 Gy and 64.5 Gy. The neutron doses were the same for all schedules. The results are shown in Fig. 5. There is no significant difference between the three mixed-fractionation schedules in clamped tumours, even allowing for the reduced X-ray doses (by 5%).

## Discussion

The present results indicate that when a population of essentially uniform oxygenation (skin or clamped tumours) is irradiated with a mixed-fractionation schedule consisting of two fractions of neutrons plus three fractions of X rays, the way in which the two types of radiation are ordered does not affect the outcome of treatment (Figs 3, 5) Nelson et al (1975) came to the same conclusion after irradiating mouse skin with mixed schedules of either NNXXX or NXXXN. In contrast, we have found that when unclamped tumours were irradiated, giving the two neutron fractions first gave greater growth delay than giving them at the end or one each at the beginning and end (Fig 2). While the difference between the schedules was small at the lowest total dose of 10.5 Gy, for all other doses giving the neutrons first was always more effective than the other mixed schedules, and equally as effective as all five fractions of neutrons. The full dose–response curve for NNXXX is significantly above those for NXXXN or XXXNN.

Since the same skin reaction was obtained irrespective of the ordering of the X-ray and neutron doses, the greater effectiveness of the schedule NNXXX when given to unclamped tumours represents a true increase in therapeutic effectiveness, at least in respect of skin, as the dose-limiting normal tissue. A way to demonstrate this increased benefit is to determine the growth delay for a given skin reaction. This simulates clinical practice when the total dose is determined by the limiting normal tissue reaction. This is illustrated graphically in Fig. 6, which shows the relationship between growth delay and skin reaction for the different fractionation schedules calculated from the dose–effect curves shown in Figs 2 and 3. Two doses of neutrons followed by three of X rays were almost equally as effective as all five doses of neutrons in causing tumour growth delay (for a given skin reaction). For instance, for a skin reaction of 0.9 the growth delay achieved by five doses of neutrons or by the mixed schedule NNXXX was about 19 days For the other mixed schedules (NXXXN, XXXNN), it was 14.5–15.5 days. Five fractions of X rays was a very ineffective schedule. At the higher skin reactions of 1 and 1 1, while the sequence NNXXX was still the best of the mixed schedules, the sequence NXXXN became the worst (Fig 6). This was somewhat unexpected because if the benefit from giving the neutrons first was because of their effect on hypoxic cells (see below), it might be expected that one neutron dose at the beginning and one at the end would be no worse than both at the end, and could be better. That this was not the case is difficult to explain and demonstrates the complexity of the factors contributing to the response of tumours to fractionated irradiation.

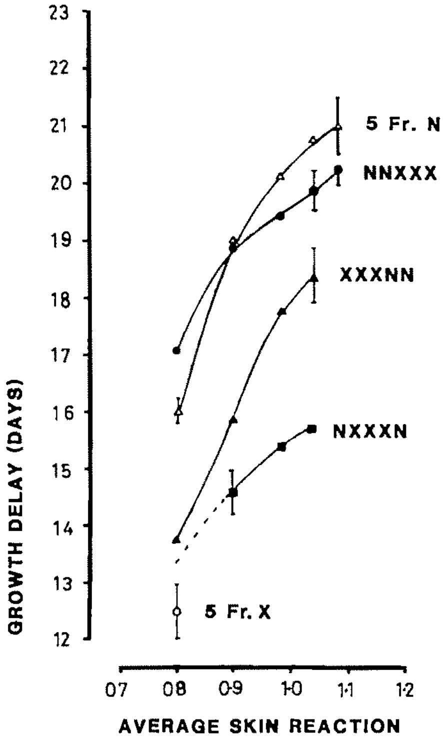

Fig 6

Tumour growth delay for given skin reactions, for fractionated irradiation

There have been two other studies of mixed fractionation in experimental systems. Nelson et al (1975) measured the response of mouse foot skin and tumour growth delay using a C3H mouse mammary carcinoma. They compared five fractions of X rays or neutrons and mixed schedules of NNXXX or NXXXN, all given 24 h apart. They expressed their results in terms of the therapeutic gain factor (relative biological effectiveness (RBE) for tumour damage relative to that for skin damage), measured at a single total dose (9.08 Gy for five fractions of X rays). This tumour underwent rapid reoxygenation so that the therapeutic gain factor for five fractions of neutrons was less than 1 (0.96). For the mixed schedules, the therapeutic gain factor was the same (1.1) suggesting a small benefit from mixed schedules, the sequencing being unimportant. In a further study, Rasey et al (1977) measured TCD50 values for the EMT6 tumour using the same schedules as in their previous study (Nelson et al, 1975). In this case the therapeutic gain factor for the schedule giving the neutrons first was slightly larger (1.3) than that giving them at the beginning and end (1.1). A value of 0.9 was obtained for five fractions of neutrons, again suggesting that reoxygenation was quite effective in this tumour.

The most likely explanation of the benefit from giving the neutrons first in a mixed schedule is that there are viable hypoxic tumour cells which persist and contribute to the outcome of treatment. Neutrons would then be effective by virtue of their reduced oxygen enhancement ratio. Model studies on the action of radiosensitisers have shown that, when they are given with only some of the fractions in a course of radiotherapy, they should be given at the beginning rather than the end of the course (Denekamp et al, 1978). This is because by reducing the *number* of hypoxic cells as quickly as possible, the number of reoxygenated survivors is kept to a minimum, irrespective of the pattern of reoxygenation Neutrons, like radiosensitisers, have their greatest effect on hypoxic cells and so the same argument would apply to them In a tumour such as that used by Nelson et al (1975), which undergoes rapid extensive long-lasting reoxygenation, the problem of hypoxic cells will be reduced so that the difference between giving the neutrons at the beginning or end will be reduced. Our observation that for clamped tumours all the mixed-fractionation schedules had the same effect (Fig. 5) supports our conclusion that the benefit from giving the neutrons first in the SaF tumour (Fig 2) is because of their greater ability to kill hypoxic cells. In clinical practice the pattern of reoxygenation in slower-growing tumours irradiated over longer periods of time than 5 days could be more extensive than is the case for the SaF tumour in the present study. Nevertheless, if neutrons are to be given at some stage in a course of fractionated radiotherapy rather than all through a schedule, our results suggest that they should be given at the beginning rather than the end.

There have been several clinical studies of the effects of mixed fractionation None of these studies specifically compared different mixed-fractionation schedules, and only one showed an advantage of mixed over conventional fractionation. In this study Maor et al (1981) treated locally advanced head and neck tumours with 60–65 Gy photons in 6–6.5 weeks, or twice a week with 0.65 Gy/fraction neutrons plus three fractions of photons per week at 2 Gy/fraction. At the time of analysis (average 22.3 months) the local control rates were 61% for the mixed-beam schedule and 25% in the photon group. Morales et al (1981) and Duncan et al (1986) found no advantage of mixed fractionation over conventional therapy for advanced carcinoma of the cervix and Grade III and IV astrocytomas respectively. Griffin and Laramore (1982) treated advanced squamous-cell carcinoma of the head and neck in a Phase I trial with neutrons alone or a mixed schedule (NXXXN) The local control rate at 2 years was 30% for the mixed-beam group and 20% for the neutrons alone. However, tumours treated with neutrons alone were more advanced than those in the mixed-beam group and the complication rates were higher.

It is clearly too early to judge from the clinical results available whether or not mixed-beam therapy might offer advantages over either photons or neutrons alone. The clinical trials which showed no advantage of mixed fractionation over conventional treatment may have done so because of inappropriate choice of neutron RBE, or because the tumours reoxygenated effectively In the astrocytoma study of Duncan et al (1986) the tumours were virtually never sterilised by photons, and neutrons alone have no benefit, so that it is not surprising that the mixed-beam schedule showed no benefit. Trials using more powerful cyclotrons offering comparable depth-dose characteristics to high-energy linear accelerators should provide more definite conclusions. Clearly, if resistant cells are limiting the probability of cure, due to hypoxia or excessive resistance of S-phase and long G1 phase cells, then high-LET radiation should be of benefit. The present study and that of Rasey et al (1977) both suggest that there might be a therapeutic gain from mixed fractionation compared with photons only, particularly if the neutrons are given first. In so far as the clinical results indicate no disadvantage from mixed-beam therapy relative to photons alone, and there may be a real advantage in certain sites, there is some reason to encourage clinicians to include a mixed-beam arm in trials of neutron therapy

## ACKNOWLEDGMENTS

We thank the Cancer Research Campaign for financial support Dr Carl is supported by Dr Mildred Scheel Stiftung, Deutsche Krebshilfe e.v, 5300 Bonn, FRG We thank Professor J. F Fowler for helpful criticisms, Mr B Hall and his team for operating the Van de Graaff accelerator, and Mr P. Russell and his staff for production and care of the animals

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1987, *The British Journal of Radiology*, 60, 589 JUNE 1987

# Technical note

## Improved localisation of the proximal end of antegrade ureteric stents

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(*Received October 1986 and in revised form December 1986*)

The use of antegrade ureteric stent insertion in patients with ureteric obstruction is well established (Pfister & Newhouse, 1979; Bigongiari, 1981; Mitty et al, 1983). The method used varies, but at Guy's Hospital the current technique involves passing a double-J ureteric stent over a Coon's guidewire. Placement is facilitated by the use of a Lunderquist Owman bile duct dilatation system (12 F sheath, 8 F Teflon dilator). When the stent is inserted as a primary procedure, a "safety" nephrostomy catheter is inserted at the end of the procedure down the track used for the stent. More frequently, the patient has had a nephrostomy catheter inserted previously via a lower-pole calyx, and stent insertion is performed via a new puncture into a more suitable middle or upper calyx.

The double-J stent (Mardis, multipurpose ureteric stent*) is supplied with a "push catheter" which is of the same radio-opacity as the stent. Consequently when the "push catheter" is advanced over the guidewire to advance the stent, it is difficult to see the proximal limit of the stent (Fig. 1).

We have found that using a flexible metal pusher ("guide rod with ball tip") from a Storz telescopic bougie set enables easier and more accurate placement of the stent (Fig. 2).

The ball tip provides a smooth pushing surface in contact with the stent and is easily visible on screening. The ball tip will pass through the 12 F sheath or down a track after 10 F dilatation.

This technique has been successfully used during eight stent insertions and has reduced the difficulty of the procedure.

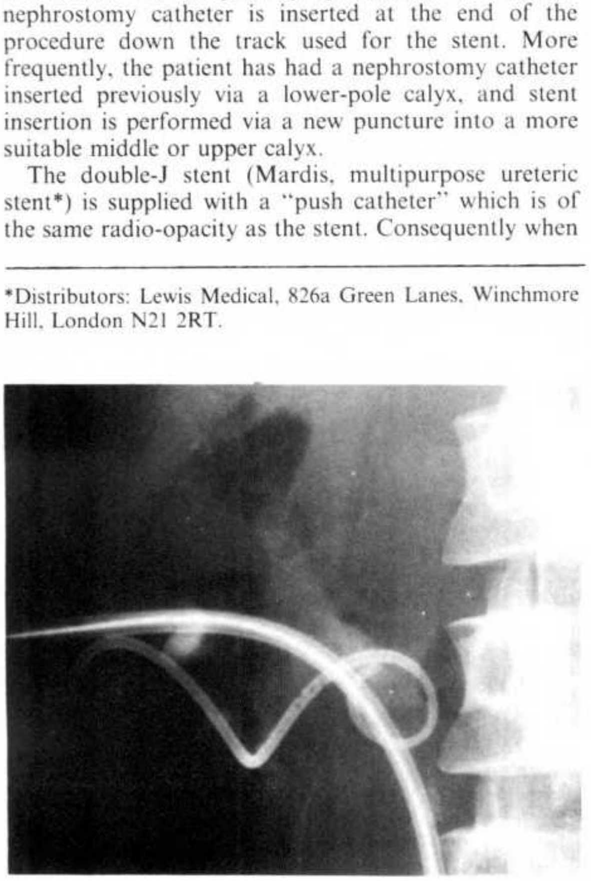

FIG. 1.

Stent insertion through a 12 F sheath. The standard "push catheter" is in place but it is impossible to see its end and so to locate the proximal end of the stent. Note the pigtail nephrostomy catheter, previously inserted via the lowermost calyx into the renal pelvis as a safety measure.

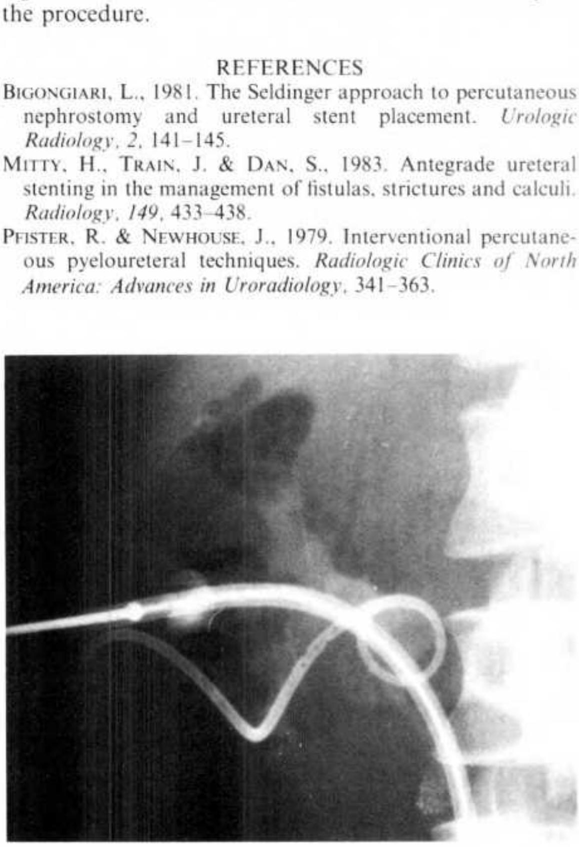

FIG. 2.

Using the Storz guide rod, the end of the stent is readily located.

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# Book review

*Radiology. Diagnosis—Imaging—Intervention.* Ed. by J. M. Taveras and J. T Ferrucci, five volumes+index, 1986 (J B. Lippincott Co, Philadelphia), £375.00+£50 for annual update.
ISBN 0-397-57115-1

What follows is a collaborative review by Addenbrooke's radiologists and physicists of the largest radiological textbook yet devised. It is in loose-leaf form, so that it can be constantly updated with fresh material New pages are promised from the start: 10–15% of the entire work is to be revised each year, says the preface.

Despite the loose-leaf form, there is nothing makeshift about the presentation of this work. It comes in five sturdy volumes, on high-quality paper, bound in well engineered folders. The size of the undertaking is impressive. The volumes weigh over 30 lb There are some 360 authors, most of them from the United States As with Grainger and Allison, the large 1986 text with whom Taveras and Ferrucci will naturally be compared, each section is masterminded by associate editors. The main subdivisions of the book are by traditional organ systems·

Volume 1· Radiologic Physics and Pulmonary Radiology,
Volume 2. Cardiac Radiology and Vascular Radiology,
Volume 3. Neuroradiology and Radiology of the Head and Neck,
Volume 4· Gastrointestinal Radiology and Radiology of the General Abdomen and Pelvis and Genitourinary Radiology, and
Volume 5. Skeletal Radiology.

The vast scale of the work is reflected by an index of 179 pages (a separate volume also to be regularly updated) and, of course, by the price Because of the cost of these books, the two British radiological journals have been asked to publish a joint review. Will libraries be tempted to take their cue from the publishers and go in for similar sharing in hard times?

The loose-leaf form appears an interesting answer to the problem of writing for a discipline that is marching fast, where textbooks age overnight. "*Radiology* will always represent the most timely major reference work in print" claims the preface We hope to be asked to report on the revision process in a year or two

T. SHERWOOD

*Volume 1 Physics*

So far only 22 of 36 chapters have been written In its present form this section cannot be considered a success Chapters are missing on too many fundamental aspects of the subject, for example X-ray generation and mechanisms of interaction of radiation with matter, for the work yet to be considered as a coherent whole The imbalance is enhanced by the fact that there are chapters on relatively specialised subjects, such as "Physical Aspects of Positron Emission Tomography" and "Fundamental Elements of Single Photon Emission Computerised Tomography"

An experienced radiologist may find chapters on specific subjects useful for refreshing the mind but, because of the large gaps, radiology trainees will be confused by information and statements that they are unable to relate to fundamental principles. There are frequent references to work "discussed elsewhere" but the relevant material is not yet available to the reader

The present chapters demonstrate both strengths and weaknesses of multiauthor volumes. To the volume's credit, each subject is presented by an expert, so the material is generally accurate, but on the other hand there are marked variations in standard and style. Thus "Basic Physics of Ultrasound Imaging" is an excellent chapter and the short chapter "Basics of Digital Computers" will allow the radiologist to speak knowledgeably over coffee about ROMs, RAMs, buses and bytes However, "Radiation Dose Calculations in Nuclear Medicine" would deter many a principal-grade physicist with its mathematical and numerical detail Also, if the two chapters on magnetic resonance merit 65 references, surely the chapter on resolution, contrast and noise deserves more than one?

Notwithstanding such criticism, much of the material is of a very high standard, and it is to be hoped that there will be an early revision of these chapters when the volume is complete, in order to establish the continuity that is lacking.

PHILIP DENDY

*Volume 1 Pulmonary*

The chest section is very good. It is comprehensive and there is uniformity of style, no doubt dictated by an excellent editor, Reg Greene. The illustrations are superb and the references plentiful, appropriate and up to date. The authors are mostly "stars" in the chest world The loose-leaf plan seems a good one to me

C. D R. FLOWER

*Volume 2· Cardiac*

One reason for so many chapters in this section (113 by some two dozen authors) is that each topic is dealt with in a number of short chapters, *e g.* mitral-valve regurgitation has separate chapters for pathophysiology, use of plain chest radiographs, echocardiography and angiography Five different authors contribute to this subject. These individual chapters are written by experts in their fields, mostly to a high standard with clearly presented texts and diagrams, and nearly all the images are beautifully reproduced. In particular, the complicated congenital heart conditions are clearly and comprehensively presented There is a welcome chapter in the introductory section emphasising the value of fluoroscopy in the detection and assessment of cardiac calcification, although its value in assessing complications of prosthetic valves should have been stated. It is also rightly emphasised how little value the technique has in the assessment of cardiac pulsation and/or motion. Despite this the abnormalities of pulsation are described in a number of the other sections, *e.g* Chapter 41 on pericardial disease. There is no chapter on the normal chest radiograph. Presumably this important omission is intended for incorporation in the "open" Chapter 2 slot?

Considering that ischaemic heart disease is so prominent in the spectrum of adult cardiac disease this subject is dealt with in remarkably few pages Coronary angiography is dealt with in a separate section towards the end of the volume and, here again, the section on occlusive disease is rather brief. One looks in vain for discussion of the techniques, complications and their prevention in coronary angiography. The names of Sones and Judkins do not appear and there is no discussion of contrast media.

The task of editing a volume with so many authors is formidable, but repetition has largely been avoided It is usually easy for reviewers to pick out minor blemishes. It is noted that the useful chapter on radiology of the post-operative chest is listed in the contents in the section on nuclear cardiology. There are some inconsistencies In the chapter on cardiomyopathy "restrictive" cardiomyopathy is not mentioned in the morphology and physiology sections. "Congestive" cardiomyopathy is described in the echocardiographic section but not elsewhere. "Azygos" is also spelt "azygous" in different sections and in Chapter 109 both spellings occur in the same paragraph. These are details Of more general concern is that among the many different chapters dealing with different imaging modalities in a given condition, it is for the most part hard to find authoritative guidance indicating the relative value of the different techniques. It is becoming increasingly necessary to be clear about which investigations will be of most benefit to the patient and reserve the use of invasive techniques, which are often more expensive and hazardous, for those conditions which cannot be adequately assessed by other means.

This volume would be a welcome addition to any radiology department specialising in cardiac investigations, despite its price. It would also be desirable in any general teaching hospital X-ray department although not necessarily the best buy if resources are short.

G. I. VERNEY

*Volume 2 Vascular*

Although Volume 2 is entitled "Cardiac and Vascular Radiology" it is almost entirely cardiac with only three vascular chapters. the remainder are spread throughout the other four volumes. This makes for quite difficult reviewing but need not deter the serious student. Some chapters are rather sketchy, *e.g* "Arteriography of the Extremities" covers the full range of pathology, investigation and intervention in 16 pages, with angioplasty getting two pages including pictures. I suspect the general radiologist would gain more from the vascular and interventional radiology section in Grainger and Allison

D. S. APPLETON

*Volume 3· Neuroradiology and Head*

Chapters 1 to 77 embrace structures above the craniovertebral junction with the accent on computed tomography, although other imaging modalities and techniques are very well covered It is refreshing that the authors have not included air encephalography: a few selected air studies are used. In general the standard of the text, illustrations and references is outstanding, with very few typographical errors. Established radiologists would find the content more than adequate, but a trainee might find it difficult to separate the "wood from the trees"

A criticism of multiauthor texts is that there may be overlap and repetition when the text is read as a whole; most chapters in this volume, however, would be studied individually. It is clear that the authors have not read each other's chapters, resulting in conflicting statements. In one chapter it is clearly stated that arteriography demonstrates the arteriopathy of neurosarcoidosis (with a reference), but later this is dogmatically denied (with an earlier review reference) There is also some variation in the style and content of the chapters but this is not serious, apart from Chapters 39 and 70, "Degenerative Diseases", which are superficial and totally lacking in organisation. In spite of these criticisms this section is a major contribution to neuroradiology and is recommended

C E L. FREER

*Volume 3· Neck and Spine*

Chapters 78 to 97, which deal with the anatomy, methods of imaging and pathology of the craniovertebral junction, the subcranial structures, the upper aerodigestive system and the thyroid, parathyroid and salivary glands, are followed by a chapter on the mode of spread of the common tumours of these tissues and of the paranasal sinuses.

Chapters 99 and 100 serve a more specialised interest· to give an account of the functional anatomy of the external carotid artery and to introduce therapeutic angiography of the head and neck.

Chapters 101 to 111 are devoted to the anatomy and pathology of the axial skeleton and spinal cord, for the most part illustrated by established imaging techniques. Chapter 112 introduces the reader to magnetic resonance imaging of the spine. The illustrations of all these chapters are well chosen and annotated. Some lack of uniformity of nomenclature and occasional typographical errors are minor blemishes in a clear, comprehensive and authoritative text, much of it contributed by authors with international reputations in their fields.

T D HAWKINS

*Volume 4· Gastrointestinal*

This section is comprehensive and well illustrated The opening chapter on plain-radiograph diagnosis is a useful reminder of the value of this simple test, which tends to be submerged in the welter of newer imaging methods. Contrast agents are dealt with in a surprisingly brief chapter, though the salient points are covered. This is followed by an excellent section on radiological-pathological correlation which should make radiologists much more aware of the nature of the changes which they are demonstrating.

Despite multiple authorship there has been surprisingly little overlap of content—proof of good editing. This section can be regarded as an admirable reference work on gastrointestinal radiology.

A. H. FREEMAN

*Volume 4: Abdomen and Pelvis*

These chapters are all written by recognised experts. Each is technically correct and highly informative Some authors have culled from their previous works and borrowed extensively from those images, giving a sense of déjà vu, while others have tried hard to write on something new. Each chapter is rather brief, akin to a collection of short stories. Maybe that is the way this book should be tackled· a topic a day to keep the examiners at bay Such brevity from a plethora of authors creates a lack of continuity and leads to inevitable repetition and overlap. This is sometimes confusing: in Chapter 68 the term THC is used for transhepatic cholangiography while in Chapter 69 it is PTC which rules. Similarly in the section on preparation for abdominal computed tomography (Chapter 57), barium and the more commonly used diatrizoate preparations are logically discussed. Then in Chapter 83 EZCAT preparation is suddenly thrust upon us Nevertheless, each chapter provides an excellent overview of the subject at hand and one which the F R C.R. candidate would do well to read. The references are almost entirely from the American literature.

A. K Dixon

*Volume 4 Genitourinary*

The work is well presented, orderly and easy to read The introduction is a lengthy but very readable account of the anatomy and techniques of examination. Some of this is elementary; descriptions of kidneys being bean shaped and an explanation of peristalsis made one wonder for whom the book was written. The remaining chapters are divided into diseases of the urinary tract, kidney, urothelium, ureter and, finally, diseases of the bladder, prostate and urethra. The anatomical approach makes for easy cross-referencing. The pathological coverage is comprehensive although rather deficient on problems of paediatric plumbing (posterior urethral obstruction and ectopic ureters), and on details of imaging in renal failure. The radiographic illustrations are good and extensive references accompany each subsection

This is a good general account of urinary tract radiology which will make extremely useful reading for F R.C R. candidates and general radiologists in everyday practice.

G Hurst

*Volume 5. Skeletal*

I am impressed by the quality of production of this memorable section The text is clear and well programmed and there are excellent illustrations The chapters are short and pungent, and the content of each is crisp and thorough. There are some missing chapters in this volume and I hope that they will be added in the next year. It was hard to find any mistakes, although the statement in Chapter 20 that there is no paediatric literature on ultrasonography of septic arthritis is now obviously incorrect. There is a good descriptive chapter on degenerative disease, but why is this still called osteoarthritis when we have no evidence for an inflammatory process? The prospect of annual renewal and insertion of new chapters is an exciting one. I have no hesitation in recommending this section

J. Tudor

*Conclusion*

Is this a new textbook we should all like to have on our shelves right now? The answers above are largely yes However, it costs 50% more than other comparable books, and my tentative personal opinion is that the work is not a' best buy (yet).

T Sherwood

1987, *The British Journal of Radiology*, *60*, 593–595 JUNE 1987

# Case reports

## Computed tomography of vinyl-chloride-induced angiosarcoma of liver

By E. J. Fitzgerald, M.R.C.P., F.R.C.R. and T. M. Griffiths, M.B., B.Ch.

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(*Received August 1986*)

Angiosarcoma of the liver is a rare tumour and carries a poor prognosis It arises from the endothelial or Kupfer cells lining the hepatic sinusoids (Buntine et al, 1971) This tumour has been linked to exposure to thorotrast, arsenicals and radium (Locker et al, 1979). It was first reported in association with vinyl chloride by Creech and Johnson (1974). Up to 1983, 95 deaths had occurred because of vinyl-chloride-induced angiosarcoma (Spirtas et al, 1983). The computed tomographic appearances of angiosarcoma of the liver have been described previously (Mahony et al, 1982; Vasile et al, 1983) but neither of these reports were of exposure to vinyl chloride or any other known carcinogen.

### CASE REPORT

A 37-year-old man presented with severe upper abdominal pain. On clinical examination there was a large mass extending from the xiphisternum to the umbilicus. An ultrasound examination showed a huge, mixed-attenuation tumour which involved the left lobe of the liver. Dynamic computed tomography (CT) was performed to assess whether the tumour was suitable for resection The non-enhanced scans showed a huge mass of mixed texture in the left lobe (Fig. 1A). Following administration of intravenous contrast medium, there was patchy enhancement of the tumour (Fig. 1B) Delayed scans, taken 15 min after injection, showed persistent patchy areas of low density, mainly centrally but also in some peripheral parts of the tumour (Fig. 1C). Other parts had become isodense with liver

The patient had worked in a local chemical plant which produced vinyl chloride. As an industrial cleaner, his duties included cleaning out the vats in which the vinyl chloride was polymerised. Exposure had lasted for 3½ years and had ceased 11 years before presentation.

He died 5 months after presentation and angiosarcoma was confirmed at autopsy.

### DISCUSSION

Angiosarcoma of the liver (which in most cases is idiopathic) has been linked to exposure to thorotrast, arsenicals and radium (Locker et al, 1979). The association between vinyl chloride and angiosarcoma was first described by Creech and Johnson (1974) and Lee and Harry (1974). The onset is insidious, with a clinical picture of non-specific hepatic injury with mildly abnormal biochemical liver function tests (Dannaher et al, 1981) Abdominal pain is the commonest symptom, followed by weakness, fatigue and weight-loss. Several asymptomatic cases were discovered during the course of a screening programme of those at risk following exposure to vinyl chloride (Locker et al, 1979).

Pathological confirmation of this tumour is difficult. Biopsy by all routes is associated with a high degree of morbidity and significant mortality. The diagnosis is usually made on the basis of tissue obtained at open liver biopsy or autopsy rather than by percutaneous or transjugular liver biopsy (Locker et al, 1979; Dannaher et al, 1981). Biopsy was complicated by bleeding, requiring multiple blood transfusions in 16% of patients in the series of Locker et al (1979). Two of the 16 patients who underwent closed biopsy died from bleeding. Thus, if the CT appearances described above are seen, open rather than percutaneous biopsy should be considered.

Treatment is usually regarded as unsuccessful although chemotherapy may prolong survival (Dannaher et al, 1981). If the tumour is confined to one lobe of liver, resection may be curative (Louagie et al, 1984) However, the average survival time after diagnosis is less than 12 months Hepatic failure and intra-abdominal haemorrhage are the usual causes of death.

Before the advent of non-invasive diagnostic imaging methods, radionuclide scans and, more particularly, hepatic angiography were used in the diagnosis of these tumours (Whelan et al, 1976). These methods showed features suggestive, but not definitely diagnostic, of this tumour (Dannaher et al, 1981; Mahony et al, 1982; Louagie et al, 1984).

Thorotrast-induced tumours appear as low-attenuation parenchymal defects in the liver (Levy et al, 1986) while idiopathic tumours show a low-attenuation mass containing some round areas of lower attenuation (Mahony et al, 1982, Vasile et al, 1983). After administration of intravenous contrast medium there is heterogeneous enhancement of the mass both peripherally and centrally (Fig. 1B). On delayed scans there is persistent low attenuation at the centre and at parts of the periphery of the mass (Vasile et al, 1983).

The absence of peripheral enhancement completely encircling the low-density area after bolus injection, together with late heterogeneous enhancement may help to distinguish this tumour from hepatic haemangioma (Vasile et al, 1983). Metastatic tumours of the liver rarely show this delayed enhancement following bolus

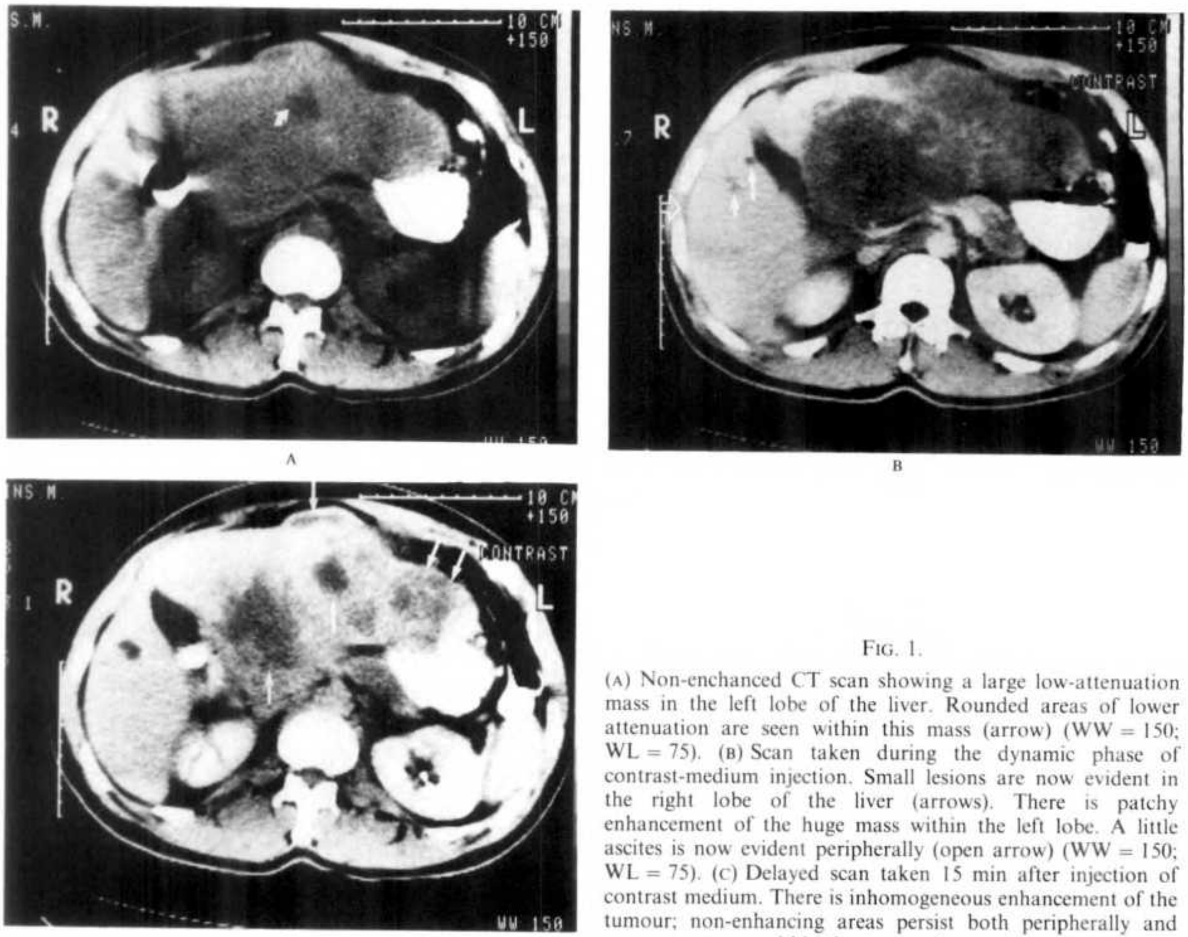

FIG. 1.

(A) Non-enchanced CT scan showing a large low-attenuation mass in the left lobe of the liver. Rounded areas of lower attenuation are seen within this mass (arrow) (WW = 150; WL = 75). (B) Scan taken during the dynamic phase of contrast-medium injection. Small lesions are now evident in the right lobe of the liver (arrows). There is patchy enhancement of the huge mass within the left lobe. A little ascites is now evident peripherally (open arrow) (WW = 150; WL = 75). (C) Delayed scan taken 15 min after injection of contrast medium. There is inhomogeneous enhancement of the tumour; non-enhancing areas persist both peripherally and within the tumour (arrows).

injection and delayed enhancement is also unusual in hepatocellular carcinoma (Vasile et al, 1983). Splenic metastases, if present, favour a diagnosis of angiosarcoma, as does the presence of spontaneous haemoperitoneum (Levy et al, 1986).

The interval between exposure to vinyl chloride and development of this tumour ranges from 12 years to 28 years. Protective measures in the working environment with reduction of atmospheric levels of vinyl chloride to one part per million was introduced only in 1974, so all vinyl-chloride-induced carcinomas may not yet have been discovered. When an apparently malignant tumour with the appearances described is found on hepatic CT, a full occupational history should be obtained, as they may be due to this rare occupational cancer.

ACKNOWLEDGMENT

We would like to thank Dr G. M. Roberts for all his advice.

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# Pulmonary embolism, haematemesis and the Gunther vena caval filter

By M. Mahendran, M.B., M.R.C.P., O. P. Fitzgerald-Finch, M.B., F.R.C.R. and D. J. Gwilt, D.M., M.R.C.P., F.F.A.R.C.S.

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(*Received August 1986*)

The management of pulmonary embolism when anticoagulation is contraindicated is a difficult clinical problem. We describe our experience of the new Gunther vena caval filter in this situation.

## CASE REPORT

A 72-year-old woman was admitted with a 2-day history of right-sided pleuritic pain, cough and dyspnoea, having had an appendicectomy 3 weeks earlier. For some years she had suffered dyspepsia, adequately controlled by antacids, and 3 years previously an endoscopy had shown a hiatus hernia with oesophageal reflux. A chest radiograph showed a right basal effusion and linear atelectasis.

A clinical diagnosis of pulmonary embolism was made and she was anticoagulated with intravenous heparin at a dose of 35 000 units per 24 h. However, after 6 h she had a haematemesis, her blood pressure dropped and her haemoglobin fell from 15.0 g/dl (measured at appendicectomy 3 weeks previously) to 9.4 g/dl. Her activated partial thromboplastin time was 56 s (control 36 s). Anticoagulation was stopped and she was given a blood transfusion. Pulmonary angiography (Fig. 1) showed a large saddle embolus lying across the bifurcation of the right pulmonary artery with hypoperfusion of the right upper lobe. At endoscopy she was found to have an oesophageal ulcer just above the hiatus hernia and this was the source of the bleeding.

Further anticoagulation was clearly inappropriate and a basket filter was inserted (Fig. 2). Under local analgesia, using the Seldinger percutaneous technique, a catheter (size 10 French gauge) was introduced into the inferior vena cava. The basket was advanced through the catheter and placed anchor first just below the renal veins, the position being confirmed by the use of contrast medium. The whole procedure took 15 min and was well tolerated.

The patient had no further recurrence of either bleeding or embolism, was discharged 2 days later and when reviewed in the outpatient department had made an excellent recovery.

## DISCUSSION

Pulmonary embolism is a potentially fatal condition which usually requires anticoagulation to prevent further embolism, but if anticoagulants are contraindicated the only alternative is to place some form of barrier in the inferior vena cava. The first successful device (Mobin-Uddin et al, 1969) was the umbrella filter, but this was associated with a high frequency of vena caval thrombosis and occasionally with migration

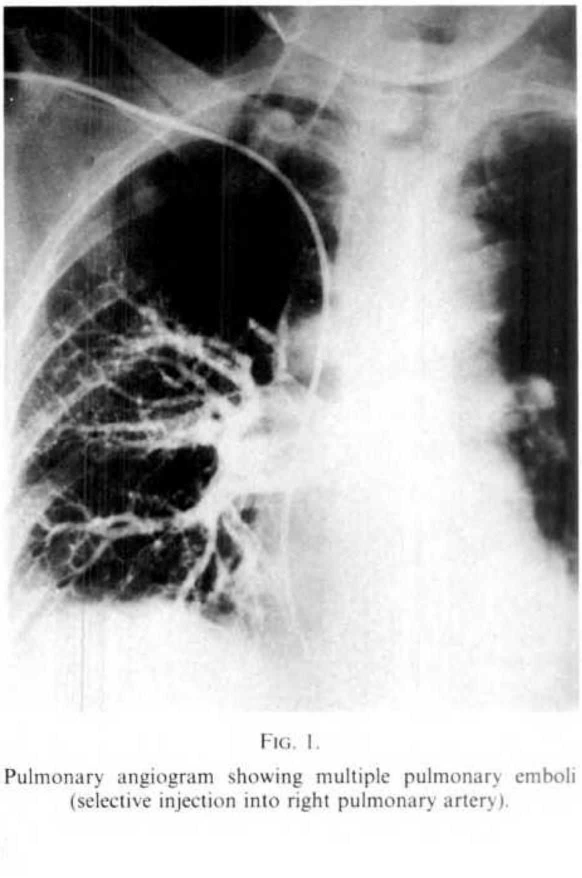

FIG. 1.

Pulmonary angiogram showing multiple pulmonary emboli (selective injection into right pulmonary artery).

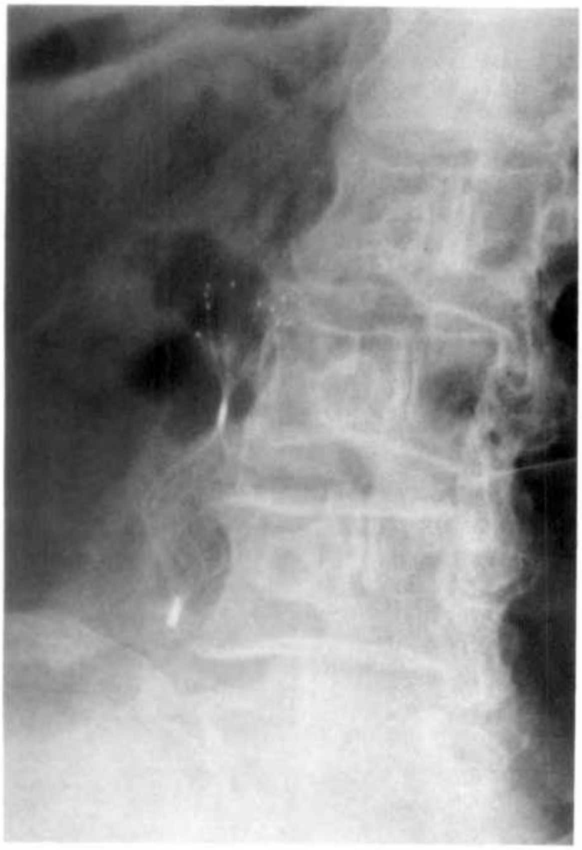

FIG. 2.

The basket filter shown lying in the inferior vena cava (oblique view).

of the device to other sites, including the pulmonary artery. The next major development was the Greenfield cone-shaped filter (Greenfield et al, 1973) but this requires considerable local venous dilatation or venotomy for its introduction. These considerations led Gunther to develop a basket filter which can be inserted percutaneously and which may have a higher rate of trapping of embolic particles than other devices (Gunther et al, 1985).

There are still relatively few reports of the use of caval filters in patients in whom pulmonary embolism is followed by anticoagulant-related bleeding (Burke et al, 1984; Rosenthal et al, 1985). In these patients it is essential to insert an effective caval barrier to further emboli, but it is equally important to do this with minimal haemodynamic upset, particularly as the combination of hypovolaemia and right ventricular outflow obstruction may critically impair peripheral perfusion. Our experience confirms that such devices are easy to implant by operators without previous experience, and that the procedure is well tolerated by the patient. Experience with the new Gunther basket filter is still limited, but our use of the device suggests that it is worthy of further consideration.

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# Case of the month

## The pre-operative chest radiograph

By S. A. Thompson, M.B., B.S., F.R.A.C.R. and J. S. Harper, M.B., B.S., F.R.C.R.

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(*Received August 1986*)

A 50-year-old housewife presented in August 1983, with iron-deficiency anaemia and bleeding per rectum. Sigmoidoscopy and barium enema were negative at that time and she underwent sclerotherapy and banding of rectal haemorrhoids.

She returned in January 1986 with lethargy due to recurrent anaemia and reported one episode of blood loss per rectum in 1985. There was no weight loss or alteration in bowel habit. Colonoscopy on February 12, 1986 showed a sessile mass at the ileocaecal valve. Biopsy of the mass confirmed invasive, moderately differentiated carcinoma.

A chest radiograph revealed a large mass in the left lung (Fig. 1) which was thought to be a secondary deposit. Computed tomography (CT) of the abdomen and chest was performed to stage the caecal tumour accurately. This revealed no other intra-abdominal disease and that the lung mass was a single lesion with no mediastinal invasion. Because the mass enhanced on CT (Fig. 2), a dynamic scan was performed through the centre of the lesion following intravenous rapid bolus injection of contrast medium, and time–density curves were generated (Fig. 3).

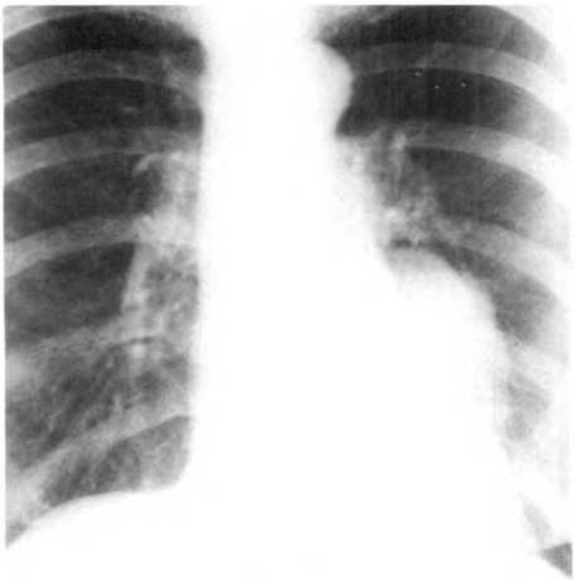

FIG. 1.

Pre-operative chest radiograph.

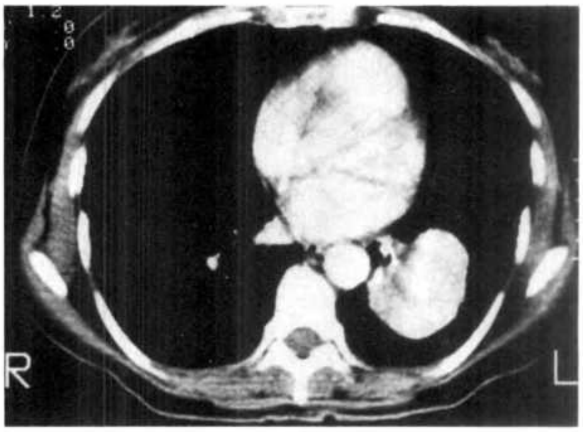

FIG. 2.

A CT scan through the pulmonary lesion.

The patient underwent a right hemicolectomy, with a left lower lobectomy 2 months later.

What do you expect the diagnosis of the pulmonary lesion to be?

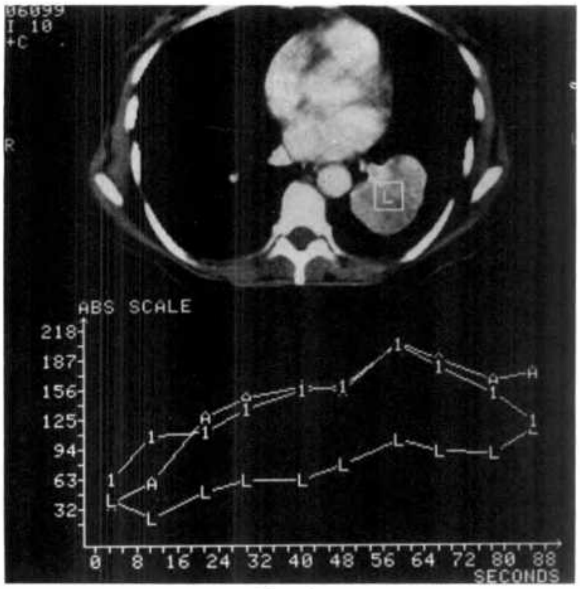

FIG. 3.

Dynamic scan showing density changes with time following injection of contrast medium (L = pulmonary mass, A = descending aorta, I = ascending aorta).

The plain radiographic finding of a well defined, centrally located single lesion is unusual for a secondary deposit, and secondaries in the lung from a primary caecal lesion without liver involvement are rarely seen. This raised the possibility that the pulmonary lesion was a second primary tumour.

For this reason contrast-enhanced CT was performed. Because of the close relationship of the mass to the lower-lobe bronchus (Fig 2) and its enhancement post-contrast, a bronchial adenoma was suspected and a dynamic study was performed. This confirmed that the mass enhanced more than normal soft tissue but less than vascular structures such as the aorta (Fig. 3). This excluded lesions such as pulmonary artery aneurysm or an arteriovenous malformation (AVM), which had also been considered

At this stage, bronchial adenoma was thought most likely and endoscopic biopsy was thought unwise. Percutaneous fine-needle biopsy was performed, which confirmed bronchial carcinoid. A little more than the normal amount of blood was aspirated during the biopsy but no complications ensued.

The histology of both the caecal and the pulmonary specimens confirmed the pre-operative diagnosis.

## CONCLUSION

The characteristic features of bronchial adenoma on CT have recently been described (Aroncheck et al, 1986). Eighty to ninety per cent of adenomas have histological features of a carcinoid. They are smooth-surfaced, well defined lesions of bronchial origin which often extend into the surrounding lung. They are characteristically very vascular and have a typical endoscopic appearance. Endoscopists have been reluctant to biopsy them because of their vascularity, so that knowledge of their characteristic features on CT is useful to radiologist, physician and surgeon in identifying them prior to percutaneous biopsy or surgery.

The characteristic location of these tumours and the association with distal atelectasis and pneumonitis have been described (Naidich et al, 1982). The enhancement characteristics present in our patient allowed differentiation from primary bronchogenic tumour and separation of tumour from distal atelectasis/ pneumonitis (Webb et al, 1983). Confusion with vascular lesions (aneurysm/AVM) may occur in some cases of marked enhancement but the use of dynamic scanning with plotting of time–density curves, as in this case, will allow differentiation in most cases (Godwin & Webb, 1981).

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JUNE 1987

# Short communication

## A new technique for renal allograft biopsy

By C. S. Ubhi, F.R.C.S., F.R.C.S.Ed., *H. C. Irving, F.R.C.R., D.M.R.D., P. J. Guillou, B.Sc., M.D., F.R.C.S. and G. R. Giles, M.D., F.R.C.S.

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(*Received December 1986*)

Renal allograft biopsy may provide diagnostic information and may be of prognostic value. However, percutaneous allograft biopsy may risk haemorrhage, infection and even graft loss (Matas et al, 1985). Various techniques have been described to minimise these risks (Nagar & Wathen, 1979; Appel et al, 1981) but some centres, like our own, have undertaken operative ("open") allograft biopsy. We present our initial experience of a new technique using an automatic spring-loaded system (Radiplast Biopty, Henleys Medical Supplies Ltd, London) guided by real-time ultrasound to localise accurately the site of biopsy.

Forty consecutive biopsies were attempted on 32 renal allografts in 32 patients. Thirty-nine patients were immunosuppressed with cyclosporin (CyA). Biopsies were only performed during episodes of renal dysfunction that could not be clearly identified as acute rejection, CyA nephrotoxicity or acute tubular necrosis. Thirty-two biopsies were performed within 6 weeks of transplantation.

Preliminary real-time ultrasonography was performed using an Elscint Dynex Sector Scanner to exclude dilatation of the collecting system and extrarenal fluid collections. The upper pole of the allograft was identified and a biopsy attachment enabled the proposed biopsy line to be projected onto the ultrasound screen. A pathway was chosen so as to maintain the biopsy needle within the cortex of the allograft (Fig. 1). The point of entry (preferably lateral to the skin incision to avoid accidental penetration through the peritoneum) was infiltrated with 1% plain lignocaine and a small skin incision made to permit easier introduction of the biopsy needle. The Biopty instrument was spring-loaded and the safety catch applied before loading the needle. The needle was passed through the channel of the biopsy attachment, and advanced through the skin incision, the renal capsule and just into the cortex of the allograft before the safety catch and trigger mechanism were released. The automatic mechanism moves the biopsy needle cannula and obturator a precise distance into the allograft in a projected line that is clearly displayed on the ultrasound image (Fig. 2).

Ten biopsies were obtained with a 14 gauge/2 mm needle and 20 with an 18 gauge/1.2 mm needle, producing 20 mm and 17 mm lengths of tissue respectively.

### RESULTS

A complete core of renal tissue was obtained at the first attempt in 38 biopsies. There was failure to obtain a renal biopsy in only one patient, 4 months post-transplant, who had a very thick fibrous pseudocapsule which prevented the needle penetrating into the allograft. A similar difficulty was encountered in one other patient 13 months post-transplant who had been converted from CyA to azathioprine and prednisolone 7 months previously. However, a complete core of cortical tissue was obtained on the second pass of the biopsy needle.

All renal biopsies were adequate for histological diagnosis although three biopsies (two 14 gauge and one 18 gauge biopsy needles) in the earlier part of this study contained mainly medullary tissue.

The procedure was well tolerated by all patients and there were no complications other than transient haematuria lasting for 12 h in one patient.

### DISCUSSION

CyA immunosuppression in renal allograft recipients has increased graft survival but it has presented new diagnostic problems in differentiating CyA nephrotoxicity from graft rejection, especially in the presence of acute tubular necrosis. Although fine-needle aspiration cytology (Hayry & von Willebrand, 1981) and intrarenal manometry (Salaman & Griffin, 1983) are new, minimally invasive procedures used to identify the cause of renal dysfunction, there are still some cases where a formal histological examination is required. This

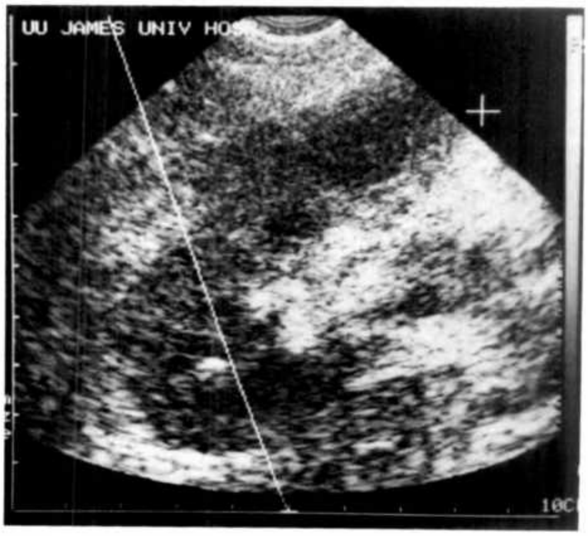

FIG. 1.

Proposed line of biopsy through the upper pole of the allograft.

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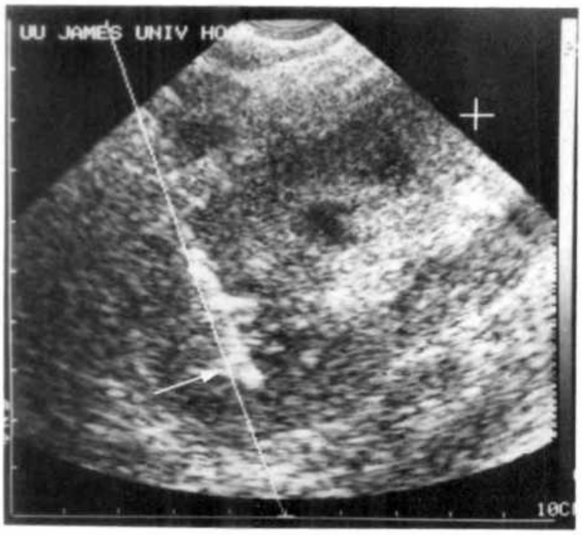

FIG. 2.

The arrow indicates the position of the biopsy needle after the trigger mechanism was released to obtain allograft biopsy.

preliminary report has demonstrated that renal allograft ultrasound-guided biopsy with the new Radiplast automatic system is a safe procedure with minimal complications, providing adequate specimens for histological evaluation. The value of ultrasound in renal allograft biopsy has been described previously (Appel et al, 1981) but this new technique offers further distinct advantages. The biopsy attachment guides the biopsy needle in the desired direction into the allograft cortex. The movement and progress of the biopsy needle can be clearly visualised by real-time ultrasonography and the automatic system has a precise movement when the trigger mechanism is released. As the biopsy needle can pass only 2.5 cm into the renal tissue along the line displayed by ultrasonography, there is minimal unnecessary trauma outside the line of biopsy.

We suggest that this technique offers a safe method for renal allograft biopsy.

## ACKNOWLEDGMENTS

We thank Mrs Jane Groves for her co-operation in the radiology department and Mrs Irene Poole for her secretarial assistance.

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JUNE 1987

# Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

## Hypoxic radiosensitisation by FLAP

THE EDITOR—SIR,

The previous report by Bales et al (1982), that 50 μM FLAP (the platinum II dichloride co-ordination complex with metronidazole) could radiosensitise hypoxic Chinese hamster ovary cells by an enhancement ratio (ER) of 2.4, cannot be substantiated either by ourselves or by others (Skov et al, 1983; Chibber et al, 1984). In order to clarify this discrepancy we have examined several aspects of the previous experimental technique, such as the level of hypoxia produced, the choice of drug solvent, the ampoules used for irradiation, the effect of FLAP on oxygen consumption and the level of non-protein thiols in the cells These studies have revealed various artefacts in the previous technique which might explain the earlier result (further details can be provided on request to Professor Nias). It is of interest that Skov (personal communication) also obtained a significant enhancement of hypoxic-cell radiosensitivity using a low dose of FLAP on one occasion but was unable to repeat the result.

We have devised a new system for rendering cells hypoxic which gives reproducible results and an oxygen enhancement ratio of 3. On testing FLAP in the new system we have found that 1 mM FLAP gives a radiation ER of 1.5 with hypoxic cells This is what may be expected in view of the fact that FLAP is more electron-affinic than metronidazole alone (Butler et al, 1985)

Yours, etc.,
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## Peripheral versus central venous contrast injection in digital subtraction angiography

THE EDITOR—SIR,

I would like to make some observations on the paper by Lea Thomas and Treweeke (1986) which attempts to compare the diagnostic image quality of digital subtraction angiograms following central venous injection with those obtained from peripheral venous injections in the same patient

There are clearly problems in the method of this study No mention is made of the possibility of bias. The 50 patients referred for digital subtraction angiography (DSA) may have been randomly selected, but this has not been stated. Indeed, the authors say that patients in whom central catheterisation was not possible were excluded from this series. We are not told why it was not possible or how frequently this occurred. The fact that 24 of the sample of 50 were being examined following femoro-popliteal bypass surgery seems to demonstrate marked sample bias, in which case a general conclusion about the suitability of peripheral injections for the whole field of DSA cannot be made "Table I" showing the "variety of vascular conditions" in the sample has been omitted from the published article.

Also in the method, the authors state "The diagnostic quality of images was then independently assessed" However, no attempt to define what is meant by diagnostic quality is made, nor is there a statement concerning who assessed the images or whether the assessor(s) were blind or double-blind If the assessment was a purely subjective one, then a study not performed blind would have observer bias which would invalidate the study

The method involved an injection rate of 15 ml $s^{-1}$. If this is the maximum rate at which an injection can be safely made into an arm vein, as the authors appear to suggest, then this would be a disadvantage of the use of peripheral injections because faster rates can be used safely with a central venous catheter, giving greater density of arterial opacification.

In the concluding paragraph, the authors state that there is no significant difference in "image quality", having previously used the undefined concept of diagnostic image quality This problem with definition of terms is reflected in the legend to Fig. 2, where the renal and visceral arteries are "not as well seen" in (A) (poorer image quality?) when compared with (B), but we are told that "the patency of the aortic graft (the clinical problem) has been established by both injection techniques". (Is this the same "diagnostic image quality"?)

In radiology, there is a trade-off between quality on the one hand and cost, radiation dose and patient safety and comfort (amongst others), on the other Central venous injections at a faster rate than employed in this study provide good-quality images without much risk to the patient. I do not believe that the slight benefit which might accrue from doing peripheral venous injections will be sufficient to persuade radiologists to change their practice unless there is proof that it will not lead to a reduction in image quality, which can only be provided by a properly constructed trial

Yours, etc.,
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## REFERENCE

Lea Thomas, M & Treweeke, P S., 1986. Intravenous digital subtraction arteriography: a comparison of peripheral versus central contrast injection. *British Journal of Radiology*, *59*, 241–244

(*Reply*)

The paper by Lea Thomas and Treweeke did not purport to be a multicentric prospective control trial of DSA quality in central venous compared with peripheral venous injections It merely made, in our view, a convincing argument that the image quality of a properly performed peripheral injection was very good indeed Assessment of image quality is always tricky and is primarily visual. It is very difficult for any radiologist to look at a contrast study and tell which concentration of contrast medium was used (within the range of iodine concentrations specified)

Again, the criticism that the authors used mainly patients who had had femoro-popliteal bypass surgery performed is ill-founded, as this merely represents the local patient population at St Thomas's, many of whom will have had this operation.

Finally, the criticism of the exclusion of patients in whom central catheterisation was not possible is again unfair, as the paper merely set out to compare image quality in those patients where both sites of injection were possible.

Editors

1987, *The British Journal of Radiology*, 60, 603–604 JUNE 1987

# Proceedings of The British Institute of Radiology

## Interventional radiology of the spine

Abstracts of papers presented at the above meeting held at Institute House, 36 Portland Place, London W1N 4AT, on Thursday October 16, 1986

**Chairman: Dr J. C. MacLarnon**

Vertebral biopsy, by D. Stoker
Embolisation of an arterio-venous fistula involving the spinal cord, by B. E. Kendall
A review of the current status of chemonucleolysis, by I W. McCall
Lower lumbar facet joint injection: a review of 245 cases, by E. N Colhoun and I. W. McCall

### VERTEBRAL BIOPSY

Dennis Stoker

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In the management of many lesions in bone, a definitive diagnosis depends on obtaining a representative biopsy specimen for pathological examination. This is important in infection, when a specific antibiotic may be necessary, in metastatic disease, when the site of the primary tumour may influence therapy and in primary neoplasia, when the nature of the cytological findings often determines the treatment. The percutaneous approach to biopsy has many advantages for the patient and the clinician, but nowhere is it so great as in vertebral biopsy, where the approach to an open surgical biopsy is, of necessity, damaging to normal overlying tissue.

The technique of vertebral biopsy, employing mainly the Jamshidi needle, is described The patient is preferably managed under sedation and local anaesthesia. Positioning of the needle is achieved in the lateral decubitus, using biplane fluoroscopy. Once the radiologist is sure that the tip of the needle is correctly positioned, several core biopsies of the affected bone are taken. It is essential that the material obtained is in a form that can be best utilised by the histopathologist Cores of bone require decalcification and hence a delay in diagnosis occurs; in all cases, touch imprint specimens are also taken, from which an earlier histological opinion may be possible. The technique is discussed in relation to the results in 135 vertebral biopsies undertaken by the author (Stoker & Kissin, 1985), of which 45 9% were for suspected infection and the remainder for suspected tumour or tumour-like conditions. No serious side-effect was encountered, even though almost half of the biopsies were in the thoracic spine The success rate was 88 1%, in 7.4% the material obtained was inadequate and in the remainder the procedure failed to result in a diagnosis for other reasons Percutaneous biopsy is increasingly being used by the radiologist on account of its accuracy, safety and cost effectiveness.

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### EMBOLISATION OF AN ARTERIO-VENOUS FISTULA INVOLVING THE SPINAL CORD

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Spinal arterio-venous fistulae are of two main types. The commonest is dural, affecting middle-aged (mean 57 years) men, 86% presenting with painful progressive paraparesis or paraplegia and 32% with eventual sphincter involvement. Such fistulae may be situated anywhere from the pelvis to the posterior fossa but most characteristically lie within the anterior part of a thoracic intervertebral foramen. Ninety-three per cent are supplied by a single artery which forms a nidus of vessels usually of small calibre (100–150 $\mu m$) draining into a single vein leading into the perimedullary venous plexus. Normal patent veins connecting the latter to the thoracic epidural venous plexus are lacking and the plexus therefore fills extensively, often draining through the upper cervical or posterior fossa veins. The mechanism of the neurological deficit is probably related to increased pressure in the perimedullary plexus causing oedema and/or ischaemic hypoxia of the spinal cord. The pressure can be reduced by excision, occlusion or by embolisation of the fistula or of the vein connecting it to the perimedullary plexus. Following embolisation, rapid improvement in symptoms occurs in about 40% (mean history 1.2 years), slow improvement occurs in another 40% (mean history 2.3 years) and 15% are unchanged (mean history 5 years) With careful patient selection complications of embolisation are uncommon (3%) but recurrence of symptoms usually associated with reopening of the fistula occurs in 60% if particles of lyophilised dura or ivalon are used and in 30% if treated with isobutylcyanoacrylate. These recurrences are generally amenable to further embolisation.

The other main type of fistula involves arteries supplying the spinal cord itself and usually the anterior spinal artery. These tend to occur in younger patients than those affected by the dural fistulae and may be either extra- or juxta-medullary (in which case they are often amenable to surgery) or intramedullary They produce progressive symptoms by increasing the pressure in the veins, draining the spinal cord and possibly by steal of blood from the cord, and also may present more acutely with cord compression and intramedullary haemorrhage. Selected fistulae of this type are amenable to particulate embolisation, occasionally, when the supplying arteries are very large, a detachable balloon technique may be the treatment of choice

### A REVIEW OF THE CURRENT STATUS OF CHEMONUCLEOLYSIS

I. W. McCall

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The enzyme chymopapain hydrolyses the proteoglycans of the nucleus pulposus in patients with prolapse through the posterior annulus, leaving a network of collagen fibres. Patient selection follows strict criteria which clinically indicate nerve-root compression confirmed as a prolapsed nucleus pulposus by radiculography or computed tomography The injection of the enzyme is performed under local anaesthetic. The needle is inserted via the lateral 60° approach, and antero-posterior and lateral screening should confirm the position in the centre of the nucleus. Contrast-medium injection is contraindicated. Chymopapain has been confirmed in randomised trials against placebo (Fraser, 1982; Javid et al, 1983). Previous clinical reviews have identified success rates of between 70% and 75% (Wiltse et al, 1975; McCulloch, 1980).

We reviewed 188 patients who have undergone chemonucleolysis. One hundred and thirty-one (70%) returned to normal activities and do not require pain killers. Twenty-four (13%) registered improvement but still had either residual leg or back pain. Finally, 33 (17%) failed to obtain any significant benefit from the injection. Of the successful patients, 70% returned to work within 6 weeks and 50% of them suffered from significant backache for more than 1 week following the injection. Laminectomy was performed on 18 patients following the injection. Seven demonstrated sequestrated discs, six had a soft-disc bulge to which the nerve root was fixed by adhesions and five had a persistent prolapse and nerve-root compression without sequestration. Seven other patients have subsequently proceeded to fusion, primarily for persistent backache. Large-disc prolapses on the radiculogram or computed tomography often fail and should proceed to surgery in the first instance. Complications have included anaphylactic shock and cauda equina syndromes, both of which are reversible by immediate treatment. Cerebral vascular accidents directly related to the enzyme have been recorded but the majority have been due to intradural injections. Finally, paraplegia has developed in the third week after the injection. The cause is not known, but the incidence is less than one in 20000. In conclusion, chemonucleolysis has proved an effective method of treatment of prolapsed nucleus pulposus. A significant failure rate, however, must be accepted. It is an alternative to surgery in most cases but, in view of the slight possibility of severe complications, it cannot be classed as a conservative means of therapy.

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## LOWER LUMBAR FACET JOINT INJECTION: A REVIEW OF 245 CASES

E. N. Colhoun and I. W. McCall

*The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire*

Two hundred and forty-five patients who presented with chronic symptoms of low back pain, with or without non-dermatomal lower limb pain referral, and in whom no previous back surgery had been performed, underwent both facet studies and provocative lumbar discography at the lower three lumbar levels. Facet studies were performed in the prone/oblique position, a 22-gauge spinal needle being inserted vertically into each facet joint under screening control. Following confirmation of an intra-articular location of the needle tip by injection of 0.1–0.2 ml of contrast medium, a further 0.4 ml of 0.5% bupivacaine was injected into each facet joint and the response of the patient's symptoms was monitored over the next 4 h. To localise accurately any level of symptom relief, only one level per day was studied in each patient. Lumbar discography was performed via the postero-lateral approach with both disc morphology and the presence or absence of symptom reproduction on contrast-medium injection being recorded at each level. In the group of patients studied, the intervertebral discs were a more frequent source of symptoms than the facet joints. Two hundred and five patients had at least one morphologically abnormal disc of which 123 (60.0%) were associated with symptom reproduction and 59 (29%) had no induced pain on contrast-medium injection. The remaining 23 patients (11%) demonstrated total disc resorption, precluding discographic examination at a particular level, but adjacent discs were not associated with symptom provocation. Forty patients had normal discs at the lower three lumbar levels. In 45 patients complete symptom relief followed injection of local anaesthetic into the facet joints. Following facet injection, no significant difference was apparent in the incidence of complete symptom relief between the three groups of patients: the incidence was 19% for those with symptomatic disc disease, 25% for those with non-symptomatic disc disease and 17% for those with total disc resorption. By contrast, of 40 patients with normal three-level lumbar discography, only two (5%) had complete symptom relief following facet injection. The study indicates that the facet joint and capsule are infrequent pain sources in patients with severe chronic low back pain, particularly when the discs are normal, but also in the presence of significant disc degeneration.

1987, *The British Journal of Radiology*, *60*, 605–608 JUNE 1987

# Accelerated fraction and hyperfractionation: experimental and clinical

## Abstracts of papers presented at the above meeting held at Institute House, 36 Portland Place, London W1N 4AT on Friday, November 14, 1986

**Chairmen: Dr J. W. Hopewell and Professor R. J. Berry**

Radiological basis of accelerated fractionation and hyperfractionation, by K R. Trott

Design and interpretation of top-up experiments, by M C. Joiner

Modelling of multiple fractions per day schedules: two or three fractions per day versus equally spaced fractions, by B. D. Michael

Repair kinetics in tumours and normal tissues, by A. M Rojas, M. C. Joiner, J Nims and H. Johns

Does the linear-quadratic model fail at low doses per fractions? by H D Thames, F. A. Stewart, K. K. Ang, A. J van der Kogel and W. Landyut

Accelerated fractionation clinical aspects, by J. F. Fowler

Human tumour cell kinetics· their role in determining the outcome of treatment, by N J. McNally and G. D. Wilson

The logistics of accelerated fractionation, by V. H J Svoboda

Treatment of cancer using multiple fractions per day over a continuous period of 12 days, by M. I Saunders and S Dische

Radiotherapy of advanced laryngeal cancer using three fractions per day, by D A. L Morgan, P J Bradley and K. A MacLennan

Accelerated fractionation. the Bavarian experience, by K. R Trott

## RADIOBIOLOGICAL BASIS OF ACCELERATED FRACTIONATION AND HYPERFRACTIONATION

K. R. Trott

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Conventional fractionation with 2 Gy per day is probably the best treatment for the average cancer patient and the majority of patients treated in this way, with curative intent, are locally cleared of tumour. However, it averages out all differences that may exist between different tumours in different patients In fractionated radiotherapy it is possible to change either the dose per fraction or the interval between fractions to improve and to individualise the fractionation schedule. Moreover, neither the dose per fraction nor the interval need be kept constant throughout the treatment period Both these components of the fractionation schedule affect different cellular mechanisms involved in the tissue response to treatment, which are well understood in tumours, much less understood in acutely responding normal tissues and very poorly understood in late-responding normal tissues, especially with regard to time-dependent effects The dose per fraction determines the amount of split-dose recovery between fractions, which may be different for different tissues and different responses in the same tissue Whereas we have little evidence that split-dose recovery may change during the course of fractionated radiotherapy, there is clinical and experimental evidence that the repopulation rate is not constant but changes considerably during the course of radiotherapy.

## DESIGN AND INTERPRETATION OF TOP-UP EXPERIMENTS

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The experimental design of a partial-tolerance radiation treatment followed by a top-up dose allows extra flexibility in dose–effect studies. It is possible to study the effects of low or clinical-sized doses per fraction, when full-course fractionation is not possible either because of the large (> 100) number of fractions required to elicit a measurable effect, or because sufficient time cannot be allocated for experimental work on clinical radiotherapy machines Neutrons are preferred to X rays as the top-up radiation, in order to minimise variations in the effect of the top-up dose For normal tissues in mice, the effect of X-ray doses as low as 0.1 Gy per fraction can be detected when given as 20–40 fractions followed by a top-up dose of d(4)-Be neutrons ($\bar{E} = 2.3$ MeV). In particular, mouse skin and kidney show a deviation from the linear-quadratic model of dose fractionation below 1 Gy per fraction, in the direction of increasing X-ray sensitivity. Top-up experiments are best implemented by giving a series of fixed initial treatments (constant fraction number and dose per-fraction) followed by a graded series of top-up doses which produce the full range of functional response Maximum resolution is obtained by maximising the number of initial "priming" fractions. Knowledge of the dose–response characteristics of the neutron top-up radiation enables data from top-up experiments and full-course fractionation to be compared directly In the X-ray dose per fraction region of overlap between the two types of experiment (≈ 2–5 Gy), there was excellent agreement.

## MODELLING OF MULTIPLE FRACTIONS PER DAY SCHEDULES: TWO OR THREE FRACTIONS PER DAY VERSUS EQUALLY SPACED FRACTIONS

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The linear-quadratic model provides a straightforward way of modelling the effects of incomplete repair during fractionated treatment (Thames, 1985; Dale, 1986) The basis of this analysis is the concept of a dose-equivalent of incomplete repair (Oliver, 1964) which accumulates at each successive fraction and decays between them with kinetics directly related to those of split-dose recovery. This paper describes a matrix method of analysing fractionated treatments which allows the effectiveness of any schedule to be modelled, including those in which the values of dose per fraction and of fraction interval are not constant throughout. The paper also compares the usefulness of the two types of fractionation experiment currently used to study repair or recovery kinetics· the two or three fractions per day schedule extended over a number of days, and the "straight-through" or "concertina" schedule which uses evenly spaced fractions. The "concertina" schedule has the advantage that it allows a greater span of isoeffect dose to be measured than with two or three fractions per day. However, it has been shown that the kinetics of recovery in "concertina" schedules are highly complex because of the multiplicity of interactions between damage produced in each fraction In addition, the escalation of the level of dose equivalent of incomplete repair in a "concertina" schedule makes it most unsuitable for experiments to determine the influence of dose per fraction on repair. These difficulties are largely avoided in experimental schedules using two or three fractions per day and these are also the best and most relevant models for the current clinical MFD treatments.

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## REPAIR KINETICS IN TUMOURS AND NORMAL TISSUES

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The repair kinetics of a mouse mammary adenocarcinoma, CANT, was compared with that of a fast-proliferating normal tissue (skin). Three fractions per day were given at various time intervals (0.5, 1, 2, 4 and 8 h) between each treatment, over a period of 5 days Repair half-times ($T_{1/2}$) were calculated using a mathematical model adapted to describe tissue responses to fractionated schedules where repair was incomplete. The results suggest that recovery from sublethal damage is faster in tumours than in skin Half-times of 0.54±0.21 h (95% CL) were calculated for tumour control probability and 1.05±0.19 h (95% CL) for acute skin reactions. The possible effect of dose per fraction on the repair kinetics was studied in a fast- and slow-proliferating normal tissue using the neutron top-up technique This allowed the very accurate determination of the effect of a constant dose per fraction of X rays Pairs of daily X-ray doses were given to both the kidneys and the skin, varying the time interval between each of the two treatments. Doses per fraction of 7 Gy or 2 Gy were studied in the kidney (given over 1 day or 9 days, respectively) and 4.4 Gy or 10.5 Gy in skin (given over 1 day or 4 days). Subsequently graded doses of neutrons were given to top-up the damage inflicted by the X-ray priming treatment. The results suggested that repair half-times vary with the size of the dose per fraction. In kidney, recovery from radiation injury was faster when the larger doses per fraction were used Half-times obtained were 0.9±0.4 h for two fractions of 7 Gy and 2.1±0.8 h for 18 fractions of 2 Gy In skin, the opposite trend was observed, *i e.* repair was faster with the smallest dose per fraction The values derived for $T_{1/2}$ were 3.3±0.6 h for two fractions of 10.5 Gy and 1.0±0.4 h for eight fractions of 4.4 Gy These studies support the idea that the half-time of recovery is dependent upon the size of the dose per fraction. However, we have no explanation as to why the trend is reversed in these two tissues

## DOES THE LINEAR-QUADRATIC MODEL FAIL AT LOW DOSES PER FRACTIONS?

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Recent evidence indicates that isoeffect doses may be overestimated for fraction sizes as low as 1–2 Gy when estimated from data obtained for fraction sizes larger than 2 Gy, for both the kidney and the spinal cord The reason for this is unknown, but possible interpretations include exhaustion of the repair capacity and incomplete repair The latter interpretation is motivated by the relatively short time intervals between twice-daily doses given to the kidney (5 h) and spinal cord (4 h) when small fraction sizes were used The possibility that overestimation of isoeffect dose could be explained by lack of complete repair during the short intervals between doses given twice daily was assessed by fitting to an appropriate mathematical model The deviation from the (complete-repair) linear-quadratic model could be interpreted for the kidney in terms of a half-time of repair of 3.2 h (although a negligibly different fit was obtained by forcing the value 1.5 h) For the spinal cord the data could be interpreted by assuming incomplete repair with a half-time of 1.7 h, which is negligibly different from the estimate obtained from repair-kinetics experiments with larger doses per fraction. If the interpretation in terms of incomplete repair is appropriate, the clinical implications are that (1) dose per fraction is not significant in determining the rate of repair and (2) MFD treatment should not be considered without intervals of 6 h or more when late reactions are dose limiting.

## ACCELERATED FRACTIONATION: CLINICAL ASPECTS

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Thirty-one published papers and abstracts on non-standard fractionation schedules were reviewed and divided into three goups, 1968–80, 1981–83, and 1984–86; Dr Svoboda was a principal investigator in the earliest group The majority of the schedules employed two or three fractions per day, and a proportion also used short overall times (2–5 weeks) Clinical evidence suggests that lengthening the overall treatment time in radiotherapy leads to lower local tumour control. From clinical trials where overall time had been altered, doubling times for clonogenic cells of about 3 days in lymphomas and 4–10 days in ear, nose and throat carcinomas could be derived. This supported the necessity for accelerated fractionation, preferably when biopsies could be performed to give individual labelling indices. Accelerated fractionation should not be done with doses per fraction larger than about 2 Gy, so multiple fractions per day are necessary The penalty of using doses per fraction of 4 Gy, instead of 2 Gy, was approximately equal to the gain to be expected by shortening treatment time from 6 weeks to 3 weeks. The minimum intervals between fractions should be about 6 h. This would avoid excessive *late* injury, because of the greater repair, which takes longer to fade to negligible levels in late- than in early-reacting tissues. This requirement makes it easier to use two fractions per day than three fractions per day in a normal working day One clinical trial had been reported in the literature with only 2 h intervals between MFD and the late reactions had been prohibitive. Ideal trials of accelerated fractionation still remain to be completed, but Drs Saunders and Dische had described a valuable one: 36 fractions over 12 days (three fractions per day), with no gap at the weekend, and with minimum intervals of 6 h A very important question in fractionation is whether 54 Gy in ~ 12 days can produce more tumour control than 64–70 Gy in ~ 5 weeks (with a short split before half the total dose is given so as to keep the overall time short)

## HUMAN TUMOUR CELL KINETICS: THEIR ROLE IN DETERMINING THE OUTCOME OF TREATMENT

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Human tumours contain both proliferating and non-proliferating cells. The parameter which describes their growth rate, *i.e.* the rate at which the cell population doubles, is the potential doubling time ($T_{pot}$). Tumours with potential doubling times less than about 5 days may be expected to undergo significant repopulation during conventional radiotherapy and could be suitable candidates for accelerated fractionation. The potential doubling time can be determined from a knowledge of the labelling index and the duration of the S-phase. Both of these parameters can be determined by flow cytometry from a single biopsy following *in-vivo* labelling with bromodeoxyuridine (BrdUrd), provided the biopsy is taken within a few hours of giving BrdUrd. From measurements of $T_{pot}$ in human tumours, using this technique, the shortest value was 46 h for a bone marrow sample from a leukaemia patient. Three "solid" tumours had potential doubling times of 99 h (carcinoma of the cervix), 118 h (carcinoma of the rectum) and 195 h (carcinoma of the stomach). This technique should make it possible to correlate cell kinetic parameters with benefit from accelerated fractionation, and so provide prognostic information in the individual patient as an aid to treatment planning.

## THE LOGISTICS OF ACCELERATED FRACTIONATION

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Over the last decade, fractionation studies have frequently used small dose increments and split-course treatments, but no determinations of proliferation rates have been attempted Even so, the results have never been inferior to daily fractionation regimes Accelerated fractionation also requires certain modifications in the organisation of radiotherapy departments, but it is more economical and convenient to the patient. It shortens the intervals between 1.5 Gy and 2.0 Gy fractions so that the overall time does not exceed 18 days Accelerated fractionation is the only logical way to use different rhythms of recovery after radiation exposure in the treatment strategy. It should be tested primarily on tumours with fast proliferation rates These dynamic characteristics are not properly reflected by conventional histology, but can be estimated by the determination of DNA synthesis "*in vivo*."

## TREATMENT OF CANCER USING MULTIPLE FRACTIONS PER DAY OVER A CONTINUOUS PERIOD OF 12 DAYS

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Accelerated fractionation, using multiple treatments in 1 day, should lead to a reduction in the extent of regrowth between fractions Using such a schedule, a pause in treatment at the week-end, or during the gap which occurs when a split course is employed, is likely to negate the benefit to be obtained. A total of 36 fractions of radiotherapy have been administered over a continuous period of 12 days with a 6 h gap between the first and second and between the second and third treatments on each day. Fifty-two patients have now been included in this Phase-I study The predicted acute reactions in the mucosa of the oral cavity and in the oesophagus were not excessive and no other immediate problems have developed Immediate tumour responses have been remarkably promising. Twelve (46%) of the 26 patients who were assessable after treatment for carcinoma of bronchus have shown complete radiological regression. This can be compared with nine (16%) of 62 similar patients included in a previous study treated in a conventional way. Fifteen patients with advanced head and neck tumours showed a rapid response in the primary site after treatment with accelerated fractionation with complete regression and healing. The technique has proved to be a practical one and the promising tumour responses, combined with the expectation of a low incidence of late changes, encourages further work.

## RADIOTHERAPY OF ADVANCED LARYNGEAL CANCER USING THREE FRACTIONS PER DAY

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Fifteen patients with Stage III and IV laryngeal squamous-cell carcinomas have been irradiated using three fractions per day, in most cases 1.1 Gy at intervals of 3 h 5 days a week, delivering at least 60 Gy over about 4 weeks To minimise the area of mucosa irradiated, prophylactic irradiation was not given to uninvolved neck nodes. Acute mucosal reactions were brisk, with confluent mucositis appearing near to the start of the third week of treatment. Four patients developed moist desquamation of the skin; in three build-up was used to avoid underdosing the pre-epiglottic space. No patient had treatment interrupted because of these acute reactions, although it was discontinued prematurely in one case, because of non-compliance. All other patients showed initial primary tumour regression Three patients needed subsequent surgery: one laryngectomy with bilateral neck dissection for residual neck disease and dysfunctional larynx (primary controlled); one laryngectomy was performed at 6 months for local recurrence, and one at 4 months for a dysfunctional but tumour-free, larynx. Post-operative healing was delayed in all three cases All other patients (11) have remained clinically tumour-free at the primary site, but one has died of distant metastases Early experience of this schedule suggests good tumour control, acceptable early reactions, but a worrying degree of late damage to normal tissues.

## ACCELERATED FRACTIONATION: THE BAVARIAN EXPERIENCE

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A study of post-operative radiotherapy of glioblastoma was performed by the Department of Neurosurgery, Gunzburg, and the Department of Radiology, Kaufbeuren One hundred and thirty-three patients were given radiotherapy, after subtotal resection of the glioblastoma, with different total doses and fractionation schedules. This included 38 patients receiving continuous accelerated fractionation with three fractions of 1.6 Gy per day, up to 60 Gy in 2 weeks The accelerated schedule was as well tolerated as the conventional schedules, but overall survival was not improved. A study on intercalating accelerated radiotherapy and chemotherapy was performed at the University Hospital, Munich. Thirty-four patients with advanced squamous-cell carcinoma of the head and neck were treated by simultaneous radio- and chemotherapy. Treatment was divided into three cycles. Chemotherapy consisted of cis-DDP 60 mg/m$^2$ intravenously, 5-FU 350 mg/m$^2$ intravenously and folinic acid 50 mg/m$^2$ intravenously on Day 2 and 5-Fu 350 mg/m$^2$ 24 h and FA 100 mg/m$^2$ 24 h on Days 2–5. Radiotherapy involved doses of 23.5 Gy divided in 13 fractions of 1 8 Gy delivered twice a day from Day 3 through to Day 11. This regimen was repeated on Day 22 and Day 44 Total radiation dose amounted to 70.2 Gy in 8 weeks. Mean follow-up was 13 (6–22) months. The survival rate was 94% and the local control rate was 82% at 1 year. Twenty-eight of the 32 achieved a complete response and four a partial response. Overall toxicity was acceptable and mucositis was not a limiting factor

1987, *The British Journal of Radiology*, 60, 609–636 JUNE 1987

# Proceedings of The British Medical Ultrasound Society

Eighteenth Annual Meeting, held at the Arts Centre, University of Warwick, Coventry, December 16–18, 1986

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## Abdominal ultrasound

**Chairman: D. O. Cosgrove**
**Co-chairman: M. Elliott**

Recent developments in paediatric abdominal ultrasound, by A. E Fried

Assessment of parenchymal liver disease· comparison of liver histology and ultrasound, by C Bland, S. H. Saverymuttu, M G. Cook, J D. Maxwell, E. J. Adam and A. E A. Joseph

Clinical value of Doppler ultrasound studies of the hepatic veins, by H. B. Meire and S. Coates

A review of the role of ultrasound and endoscopic retrograde cholangiopancreatography in the management of biliary and pancreatic diseases in a district general hospital, by D. Chand, R. M. Donavan and G. V. H. Bradby

Benign pancreatic insulinoma: pre-operative and intraoperative sonographic localisation, by B. Gorman, J. W. Charboneau, E. M. James, C C. Reading, A. K Galiber, C. S. Grant, J A. van Heerden, R. L. Telander and F. J. Service

The ultrasonic assessment of local complications of percutaneous renal stone removal, by C. Ivory, P Dubbins, I. P. Wells and J. Hammonds

The staging of rectal cancer. a comparison of clinical and radiological techniques, by J. Beynon, N. J. McMortensen, D. M. A. Foy, J. L. Channer, J. Virjee and P. Goddard

Prostatism. why do an intravenous urogram? by R. A Byrne, C. A. McConnell and C. H Wright

Endosonographic assessment of lateral tumour extension in rectal tumours, by J. Beynon, D. M. A Foy, J. L. Channer, J Virjee and N. J. McMortensen

Ultrasound identification of oesophageal varices: comparison with endoscopy, by S. H. Saverymuttu, C. Bland, C Ward, J. D. Maxwell and A. E. A. Joseph

### RECENT DEVELOPMENTS IN PAEDIATRIC ABDOMINAL ULTRASOUND

A. E. Fried

*Albert B Chandler Medical Center, Kentucky, USA*

Initial evaluation of masses in the new-born and infant abdomen is logically the province of sonography. The most common palpable mass in the new-born abdomen is a congenital multicystic kidney. Cysts of varying sizes without an essentially dominant cyst usually distinguishes this entity from hydronephrosis. When doubt persists, percutaneous puncture under sonographic guidance will clarify the situation.

Percutaneous nephrostomy placement in cases of ureteral pelvic-junction stenosis is also accomplished under ultrasound, frequently in the neonatal and intensive care unit. The absence of kidney, as in Potter's syndrome, or identification of the large echogenic kidneys of infantile polycystic disease will be crucial in management decisions.

Developmental difficulties in the gastrointestinal tract are also properly approached with ultrasound. Jaundice may well be due to neonatal hepatitis but demonstration of fusiform (or saccular) dilatation of the common bile-duct allows the diagnosis of choledocal cyst. Duplication cysts of the gastrointestinal tract, chiefly duodenum or colon, appear as ovoid cystic or complex masses. Signs of intestinal obstruction and a cystic or complex mass raise the suspicion of a meconium pseudocyst secondary to perforation *in utero*. Thickening of the hyperechoic muscular wall of the pylorus beyond 5 mm reinforces the clinical diagnosis of hypertrophic pyloric stenosis A similar clinical picture can be produced by an annular pancreas, which may be identified sonographically as a soft-tissue fornice lateral to the descending duodenum

Sonographic evaluation of the female genital tract in the infant centres around identification and characterisation of ovarian masses and investigation of the infant with ambiguous external genitalia to confirm the presence or absence of a recognisable uterus

In short, ultrasound may provide the definitive diagnosis in many situations in the paediatric abdomen and will at least serve to direct an effective work-up plan.

## ASSESSMENT OF PARENCHYMAL LIVER DISEASE: COMPARISON OF LIVER HISTOLOGY AND ULTRASOUND

C. Bland, S. H. Saverymuttu, M. G. Cook,
J. D. Maxwell, E. J. Adam and A. E. A. Joseph

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The accuracy of ultrasound in identifying steatosis (fat) or fibrosis in diffuse parenchymal liver disease is controversial for two reasons. Firstly, the ultrasonic characteristics of fat and fibrosis in the liver are in dispute, particularly over whether fat or fibrosis is associated with beam attenuation. Secondly, in previous histological comparisons with ultrasound there has been an interval between the liver biopsy and ultrasound of several days or even weeks, during which the degree of steatosis in particular could change. We have used clearly defined ultrasound criteria for both fat and fibrosis in an ongoing comparative study with histology, where liver biopsy was performed within 24 h of the ultrasound. Forty patients with suspected liver disease have so far been studied. Using a 5 MHz transducer, the most important criterion for steatosis was beam attenuation. A fine hyperechogenic pattern and loss of portal-vein wall echoes were usually apparent. Fibrosis by itself was recognised by a coarse, hyperechogenic pattern without loss of portal-vein wall echoes or any beam attenuation. The presence of fibrosis within a fatty liver was recognised by identifying focal high-intensity echoes in the fine hyperechogenic background.

Histology showed fibrosis in 23 (15 cirrhotic/eight pre-cirrhotic) and 27 had excess fat. Ultrasound had a sensitivity of 87% in identifying patients with fibrosis, including all 15 with cirrhosis. There were two false positives, giving a specificity of 88%. For steatosis sensitivity was 96% with a specificity of 92%. In 18 patients with both fat and fibrosis, both were correctly identified in 14 (sensitivity 78%). On the basis of these results we conclude that with a 5 MHz transducer steatosis and not fibrosis is associated with beam attenuation and that ultrasound compares well with histology in the identification of steatosis and fibrosis.

## CLINICAL VALUE OF DOPPLER ULTRASOUND STUDIES OF THE HEPATIC VEINS

H. B. Meire and S. Coates

*Kings College Hospital, London*

Examination of the blood flow patterns in the hepatic veins was initially studied, incidentally, during examination to study the portal-vein blood flow. Complex bimodal pulsations were observed in the hepatic veins in the normal patient. Marked changes in these patterns were observed in patients with a variety of liver, cardiac and intra-abdominal abnormalities. The factors affecting the hepatic-vein blood flow pattern have been studied and the specific changes in earlier liver disease have been elucidated. In addition, a number of non-hepatic causes of false positive diagnosis of liver disease have been noted.

## A REVIEW OF THE ROLE OF ULTRASOUND AND ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY IN THE MANAGEMENT OF BILIARY AND PANCREATIC DISEASES IN A DISTRICT GENERAL HOSPITAL

D. Chand, R. M. Donavan and G. V. H. Bradby

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The ultrasound and endoscopic cholangiopancreatography findings in 100 consecutive patients with symptoms referable to the biliary tract and pancreas are presented. The relative merit and uses of each examination are discussed with reference to the role of ultrasound-guided puncture of biliary tree and papillotomy in management of these patients.

## BENIGN PANCREATIC INSULINOMA. PRE-OPERATIVE AND INTRAOPERATIVE SONOGRAPHIC LOCALISATION

Brian Gorman, J. William Charboneau, E. Meredith James, Carl C. Reading, Angelo K. Galiber, Clive S. Grant, Jon A. van Heerden, Robert L. Telander and F. John Service

*Mayo Clinic and Mayo Foundation, Rochester MN, USA*

Twenty-nine patients with surgically proved benign pancreatic insulinoma were studied by pre-operative and/or intraoperative sonography. Twenty-five patients had solitary pancreatic tumours and four had multiple tumours. Six of the patients with solitary insulinomas and one of the patients with multiple insulinoma had undergone previous, unsuccessful exploration for insulinoma. Pre-operative sonography was performed in 24 patients with solitary insulinomas and 15 of the 24 tumours were localised (63%). Intraoperative sonography was performed in 22 patients with solitary insulinomas, and 19 of the 22 tumours were visualised (86%) without the knowledge of the location by prior palpation. Four of these visible solitary tumours (18%) were not detected by palpation at operation.

All the solitary insulinomas were detected with the combination of palpation and intraoperative sonography. In each of the six patients with solitary insulinoma who had undergone previous operation, the tumour was visible with intraoperative sonography. Intraoperative sonography demonstrated non-palpable insulinomas in two of the four patients with multiple tumours.

Pre-operative real-time sonography is a sensitive, non-invasive, inexpensive method for localisation of insulinoma. Intraoperative high-frequency sonography is a highly sensitive method for the detection of insulinoma. Intraoperative sonography is also valuable to determine the relationship of the insulinoma to pancreatic and bile ducts and thereby facilitates safe enucleation.

## THE ULTRASONIC ASSESSMENT OF LOCAL COMPLICATIONS OF PERCUTANEOUS RENAL-STONE REMOVAL

C. Ivory, P. Dubbins, I. P. Wells and J. Hammonds

*Plymouth General Hospital*

Percutaneous renal-stone removal has become an accepted method for removal or destruction of calculi within the renal pelvis and upper ureter. Haemorrhage, both primary and secondary, is a known complication rarely needing surgical intervention but necessitating transfusion in around 1.5–6% of cases. Extravasation of irrigation solution containing glycine is known to cause water intoxication. On rare occasions the pelvicalyceal system is known to be perforated at the time of the procedure at a site away from the operative tract. Ultrasound is known to be a sensitive method for the detection of fluid collection. The aim of this study was to assess the incidence of peri-renal fluid collection and to attempt to characterise these collections, to follow their resolution and later to quantify renal scarring following the formation of the large parenchymal tract required for the procedure.

A prospective study has been performed. Approximately one percutaneous renal-stone removal is performed weekly at Derriford Hospital in the X-ray suite under general anaesthesia. Ultrasound examination was performed using an ATL 100 sector ultrasound scanner, the base-line examination being performed on the day of admission. Further examinations were performed immediately after the procedure, a few days later, before removal of the pig-tail catheter, and a late follow-up examination at approximately 2 months after the procedure. Further examination may be performed at intervals for clinical indications.

The method of ultrasound examination together with associated technical difficulties are described. The incidence, ultrasound appearance and time to resolution of peri-renal fluid collections will be presented. In addition, other complications of the procedure, demonstrated by ultrasound, are illustrated. The role of ultrasound in the assessment of local complications and in the immediate and long-term follow-up of renal calculous disease treated by percutaneous removal is discussed.

## THE STAGING OF RECTAL CANCER: A COMPARISON OF CLINICAL AND RADIOLOGICAL TECHNIQUES

J. Beynon, N. J. McMortensen, D. M. A. Foy, J. L. Channer, J. Virjee and P. Goddard

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Forty-four patients with primary rectal cancers have been examined pre-operatively digitally, with endorectal sonography and with computed tomography (CT). Digital examination had an overall accuracy of 68% and predicted invasion beyond the muscularis propria with a sensitivity of 68%, a specificity of 83%, positive predictive value of 100% and negative predictive value of 46%. In comparison, CT had an accuracy of 82%, a sensitivity of 86%, a specificity of 62%, positive predictive value of 91% and negative predictive value of 50%. Endorectal sonography is a highly accurate way of staging local invasion and when compared with post-operative histopathology had an overall correlation coefficient of 0.84 ($p < 0.001$) (Rank Spearman). In addition, its accuracy was 91% and it could predict invasion beyond the muscularis propria with a sensitivity of 94%, specificity of 87%, positive predictive value of 97% and negative predictive value of 78%. Pre-operative assessment with endorectal sonography accurately stages the local invasion of rectal tumours and is more accurate than more conventional methods of assessment such as digital examination and CT.

## PROSTATISM: WHY DO AN INTRAVENOUS UROGRAM?

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Since October 1985 over 100 patients with symptoms of prostatism have had an intravenous urogram and ultrasound examination on the same day, including per rectal examination of the prostate using a linear-array endoprobe (Sonoline, Siemens). The findings and relative merits of the two examinations in the evaluation of prostatism are discussed, including a cost-effect analysis of the two procedures.

## ENDOSONOGRAPHIC ASSESSMENT OF LATERAL TUMOUR EXTENSION IN RECTAL TUMOURS

J. Beynon, D. M. A. Foy, J. L Channer, J. Virjee and N. J. McMortensen

*Departments of Surgery, Medical Physics, Pathology and Radiology, Bristol Royal Infirmary*

Malignant fixation in rectal tumours is associated with a worse prognosis and, particularly, a higher incidence of local recurrence. However, distinguishing between these two types of fixation by digital examination is difficult. Using endoluminal ultrasound (ELU) we have compared pre-operative ultrasonic measurements of the depth of invasion with histopathological estimates measured from both prepared sections and operative specimens. Ultrasonic examinations were performed with a rotating endoprobe using 5.5 MHz and 7.0 MHz transducers, selecting images at the site of maximum tumour depth.

In 35 patients a comparison was made between tumour depth on ELU and depth measured from the histological section. The coefficient of correlation was 0.63 ($p < 0.001$). In 27 patients it was possible to compare ELU with tumour depth measured from the resected specimen, giving a coefficient of correlation of 0.80 ($p < 0.001$).

Pre-operative ELU assessments of the depth of invasion of rectal tumours are accurate when compared with histology. Thus ELU may provide an objective method for differentiating between inflammatory and malignant fixation which will be of use in the planning of surgical strategy and also of trials of adjuvant therapy.

## ULTRASOUND IDENTIFICATION OF OESOPHAGEAL VARICES: COMPARISON WITH ENDOSCOPY

S. H. Saverymuttu, C. Bland, C. Ward, J. D. Maxwell and A. E. A. Joseph

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The recognition of oesophageal varices in patients with chronic liver disease is important, since it firstly identifies those patients liable to the complication of variceal haemorrhage and secondly indicates portal hypertension and usually progression to cirrhosis has occurred. Currently, endoscopy or radiography are used to screen for varices. Since ultrasound is routinely used as the initial assessment of chronic liver disease, the recognition of oesophageal varices at this time would aid both investigation and management. Several attempts have been made to predict the presence of oesophageal varices by ultrasound using indirect methods such as portal-vein diameter and failure of the normal respiratory variation in portal-vein size. These are, however, associated with low specificity. We have attempted to visualise oesophageal varices directly by ultrasound examination of the lower oesophagus.

In a prospective comparative study with upper gastrointestinal endoscopy, 90 patients with suspected or proven liver or biliary tract disease were examined by ultrasound. Oesophageal varices were recognised on ultrasound by thickening of the oesophageal wall, irregularity of the air-containing lumen and variation in oesophageal wall thickness during breathing. In seven patients ultrasound was unable adequately to visualise the oesophagus, while in four patients endoscopy was equivocal as to the presence of oesophageal varices. Excluding these two groups, ultrasound detected 17 out of 20 oesophageal varices (sensitivity 85%) while incorrectly suggesting varices absent on endoscopy in four patients (specificity 93%). We conclude that ultrasound can identify oesophageal varices with high sensitivity and specificity and should be specifically sought in all patients with suspected chronic liver disease.

# Physics and interaction of ultrasound with tissue

**Chairman: C. R. Hill**
**Co-chairmen: J. Pelmore and P. J. Roberts**

Ultrasound: considerations for its safe and appropriate use, by G ter Haar
The measurement of the acoustic output of medical ultrasound equipment and its implementation using a rapid quantitative on-line technique, by D. J. Locke
Heat production by a strongly focused ultrasound beam, by R L Clarke, G ter Haar, C R Hill, M Sambrook and W Swindell
Characterisation of the acoustic field generated by a Dornier extracorporeal shock-wave lithotripter, by A. J. Coleman
Anti-inflammatory and pro-inflammatory mechanisms of therapeutic ultrasound, by I. Hashish and W. Harvey
Ultrasound-induced changes in electrical pain threshold perception in humans, by A R Williams, M Bowditch and J. McHale
Investigations into the effect of ultrasound on spontaneous transmitter release at the frog neuromuscular junction, by W J Revell and M Roberts
Correlation of sonoluminescence with the standing-wave component of an acoustic sound field produced by a therapeutic unit, by T. G. Leighton, M. J W. Pickworth and A J. Walton
A study of ultrasonic pulse-echo beam-hardening using tissue-mimicking test objects, by R. Price and J. A. Evans
Computer-controlled gain compensation in ultrasonic imaging, by S D. Pye, S. R Wild, W. N McDicken and S Mackenzie
Applications of a new visualisation system, by J. Szilard
A non-linear space-varying technique to reduce speckle in ultrasonic images, by T Loupas, W N. McDicken and P L. Allan
Analysis and filtering of ultrasonic speckle, by J C Bamber

## ULTRASOUND: CONSIDERATIONS FOR ITS SAFE AND APPROPRIATE USE

Gail ter Haar

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It is undoubtedly true that ultrasonic techniques represent a large and increasing benefit to mankind, and this is particularly true in the medical field At power levels sufficiently high to modify, damage or destroy human tissues, ultrasound is employed for many therapeutic and surgical applications At lower power levels, it is an indispensable diagnostic modality It is difficult to build up a systematic and complete account of all the possible effects and mechanisms that might lead to undesirable consequences of ultrasonic exposures, and as such it is impossible to predict fully all the conceivable consequences of human exposures. In the 25 years during which medical ultrasound has been used, no verifiable indication has arisen of any adverse effect of its use, either in diagnostic procedures or in properly controlled therapy In the current situation, therefore, where risk of injury is extremely slight, and benefit of some kind is generally expected, it seems helpful to try to define conditions and working practices that are "appropriate" to the application being considered. Relevant criteria are presented for a variety of different practical situations in an attempt to justify the suggested "appropriate" conditions for "safe" usage. These concepts are detailed in a WHO publication (ter Haar & Hill, 1987)

### REFERENCE

TER HAAR, G R. & HILL, C. R., 1987 Non ionizing radiation protection In *Ultrasound,* Chapter Four, (World Health Organization, European Office), in press.

## THE MEASUREMENT OF THE ACOUSTIC OUTPUT OF MEDICAL ULTRASOUND EQUIPMENT AND ITS IMPLEMENTATION USING A RAPID QUANTITATIVE ON-LINE TECHNIQUE

D. J. Locke

*Ultrasound Dosimetry, Nuclear Enterprises Limited, Beenham, Reading*

This lecture outlines the current status of measuring the acoustic output of medical ultrasound equipment with a description of a system that can rapidly assess acoustic outputs from ultrasound transducers. This quantitative technique can be used to characterise the transducers used in medical imaging, Doppler and physiotherapy equipment. The data acquired allow on-line calculations of all the recognised acoustic parameters in accordance with AIUM/NEMA, FDA and draft IEC standards.

## HEAT PRODUCTION BY A STRONGLY FOCUSED ULTRASOUND BEAM

R. L. Clarke, G. R. ter Haar, C. R. Hill, M. Sambrook and W. Swindell

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Experimental tests have been made of previous theoretical predictions (Swindell, 1985) that in the presence of substantial non-linear propagation, a strongly focused ultrasound beam will show significant enhancement (over linear conditions) in the rate of energy deposition near the focal region Investigations have been made at 0.56 MHz and 1.74 MHz, using a 12.5 cm-diameter plane PZT transducer and a biconcave perspex lens that together gave a beam with an approximately Gaussian profile, a focal length of 13.6 cm and a pressure FWHM at the focus of 0.55 cm. Evidence for non-linearly-induced enhancement was sought in a series of experiments in which thermocouple measurements of temperature rise in the vicinity of the focus were made in various materials, including agar, ox and pig liver and some elastomers. Constant time-average power was maintained as the peak intensity was varied by changing the mark : space ratio in tone-burst conditions. Non-linear enhancement has been seen in agar and possibly in elastomers at 0.56 MHz. At 1.74 MHz (but not at 0.56 MHz) evidence of non-linear behaviour was detected in liver at pressures above 0.6 MPa. Some narrowing of the beam at the focus was also seen

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# *Proceedings of The British Medical Ultrasound Society*

## CHARACTERISATION OF THE ACOUSTIC FIELD GENERATED BY A DORNIER EXTRACORPOREAL SHOCK-WAVE LITHOTRIPTER

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Voltage waveforms in the acoustic field generated by a Dornier shock-wave lithotripter have been measured using a bilaminar shielded PVDF-membrane hydrophone in water. Various characteristic features of the measured waveform are noted, including a shock front which rises to a peak positive voltage in less than 30 ns. The peak positive voltage decays in around 1 μs, goes negative and finally recovers to zero in about 3 μs. Peak positive and negative voltages were recorded from the waveforms and the peak positive ($\hat{p}+$) and peak negative pressures ($\hat{p}-$) have been estimated from these voltages. At the focus $\hat{p}+$ is found to be 38.6 (SD±9) and $\hat{p}-$ is 10.1 (SD±1). Values of $\hat{p}+$ and $\hat{p}-$ are found to fall to 50% (6 dB level) of the focal values in a cigar-shaped region centred on the focus and extending about 60 mm along the major axis of the reflector with a maximum width of 20 mm. A large (25%) variation between the measured peak voltages, owing to successive electrical discharges, is attributed to the inherent variability of the strength and exact location of electrical discharge, and this is found to be the dominant source of error using a single-element hydrophone for characterising the acoustic field. Evidence of significant amounts of cavitation occurring in the water around the focal region is also presented, along with evidence of damage to various materials placed in the path of the shock wave.

## ANTI-INFLAMMATORY AND PRO-INFLAMMATORY MECHANISMS OF THERAPEUTIC ULTRASOUND

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Ultrasound therapy is widely used to reduce acute inflammation in soft-tissue injuries, but very few controlled studies have attempted to test its effectiveness. We have investigated (i) the extent and nature of anti-inflammatory activity of "therapeutic" ultrasound following minor oral surgery and (ii) the effects of ultrasound on mast cells *in vitro*.

Post-operative inflammation was assessed by measurement of facial swelling with a face bow device, limitation of mouth opening, pain score, and the acute phase serum C-reactive protein (CRP) 24 h after surgery. In a double-blind placebo-controlled trial the lowest intensity of ultrasound (0.1 W cm$^{-2}$) given 4–6 h after operation reduced all the measurements of inflammation by about 50% compared with untreated controls, but higher intensities of ultrasound were progressively less effective. The placebo- ("mock" ultrasound) treated group also showed a similar significant reduction in inflammation. A second clinical trial showed that this was a true placebo effect and not related to the massaging movement of the ultrasound applicator. *In-vitro* experiments showed that ultrasound caused histamine release (measured by single-isotope enzyme assay) from rat peritoneal mast cells. Degranulation was related to ultrasound intensity over the therapeutic range (0.1–1.5 W cm$^{-2}$) and was temperature dependent, occurring at 37°C but not 25°C. Addition of EDTA and antimycin A inhibited ultrasound-induced degranulation, indicating it was calcium- and energy-dependent and not a non-specific effect. The pro-inflammatory effects of higher ultrasound intensities found in the clinical trial may therefore be attributable to histamine release. The results indicate that ultrasound therapy can significantly reduce post-operative inflammation, but that this is a placebo effect, and independent of the ultrasound itself. It is possible that the analgesic effect of mock ultrasound, in common with other types of placebo therapy, is due to release of endogenous opioids.

## ULTRASOUND-INDUCED CHANGES IN ELECTRICAL PAIN THRESHOLD PERCEPTION IN HUMANS

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Two wire electrodes, each 0.2 mm in diameter and 8 mm long, were attached 8 mm apart to the skin of the forearm of young adult volunteers by means of an acoustically transparent plastic adhesive tape. The volunteer increased the voltage of the rectangular electrical pulses supplied to the electrodes until a reproducible sharp prickling pain was felt. A 1 inch diameter physiotherapy transducer driven at 1.1 MHz or 3.3 MHz (EMS Therasonic 1030) was clamped and held in light contact with the forearm centred over the 8 mm × 8 mm electrode site. The volunteers wore blindfolds and headphones which played loud music, and were not aware if any given pain threshold measurement was a test or a control. Preliminary experiments established that highly reproducible (typically ±3–4%) pain threshold values could be obtained and that these values were not affected by small changes in: the duration of the "on" time of the electrical pulses; the time interval between successive threshold measurements; the contact pressure between the transducer and the electrode site, or whether or not a test measurement was preceded by a control. A second person (the observer) had the sole responsibility for choosing the experimental protocol, timing the interval between measurements, recording the threshold measurements, resetting the equipment, and energising the transducer during the test series of measurements.

Ultrasound exposure consistently produced a statistically significant ($p < 0.05$) decrease in the threshold for the perception of electrical pain. The magnitude of this effect increased with both increasing intensity (rising to −20.7±0.57% at an SATA intensity of 0.43 W/cm$^2$ at 1.1 MHz, continuous wave) and increasing frequency of the ultrasound. Delivering the same amount of ultrasonic energy in the form of bursts 2 ms long at several different peak intensities produced exactly the same reduction in pain threshold perception. These results indicate a thermal mechanism and similar results could be obtained by heating or cooling the electrode site by non-acoustic means. Five extended series of control and test investigations were also performed using continuous-wave 3.3 MHz ultrasound at an SATA intensity of 10 mW/cm$^2$ (with an uncertainty of about ±3 mW/cm$^2$). Each individual series gave a statistically significant ($p < 0.05$) reduction in the perceived pain threshold, and the percentage reduction averaged over all the series was 4.52±1.15%. The minimum amount of ultrasonic energy which had to be delivered before we could detect a change in the perceived threshold was about 1 J/cm$^2$ and the total amount delivered in each of the five series was about 3 J/cm$^2$. These extremely low-intensity values for a reproducible ultrasound bioeffect reflect the use of a sensitive functional (sensory) end-point and do not imply a potential hazard.

## INVESTIGATIONS INTO THE EFFECT OF ULTRASOUND ON SPONTANEOUS TRANSMITTER RELEASE AT THE FROG NEUROMUSCULAR JUNCTION

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The past 10 years have seen a growing appreciation of the importance of ultrasound therapy in the effective treatment of a variety of physical disorders, including ankylosing spondylosis, muscle and tendon strains and trophic ulcers. The biological effects of ultrasound are often separated into thermal and non-thermal mechanisms, although these should be viewed as operating at either end of a continuum and not as discrete phenomena. Non-thermal modes of ultrasound are currently attracting a great deal of attention and evidence is accumulating that some of the observed biological interactions are produced as a result of physical perturbation of cell membranes induced by cavitation and microstreaming.

We have examined the effect of low-level ultrasound (0.25 W/cm$^2$, 1.5 MHz, continuous wave) on the spontaneous release of acetylcholine at the frog neuromuscular junction. These events give rise to miniature end-plate potentials (MEPPs) which may be recorded intracellularly from the post-synaptic muscle cell. Using a simple chamber in which the muscle preparation was secured to a polyurethane resin baseplate it was found that 3 min of exposure to ultrasound of the stated parameters resulted in a significant increase in the frequency of MEPPs, with only small concomitant increases in temperature (1.0–1.6°C). Control experiments involving the same temperature rises gave only small increases in MEPP frequency and these results were similar to those reported by other investigators. However, these experiments were repeated using a more sophisticated exposure apparatus. In this device the muscle was suspended across a gap over an acoustically transparent window. The inner chamber was contained within a thermostatically controlled water bath, lined with an acoustically absorbent material. There was, thus, little possibility of reflection or standing-wave phenomena occurring. In this more controlled experiment we have *not* been able to demonstrate conclusively the effects shown in the earlier work, although the temperature increase recorded from a thermistor probe close to the muscle preparation was very similar in both magnitude and time course.

## CORRELATION OF SONOLUMINESCENCE WITH THE STANDING-WAVE COMPONENT OF AN ACOUSTIC SOUND FIELD PRODUCED BY A THERAPEUTIC UNIT

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When small bubbles are subjected to ultrasound at sufficiently high intensities, unstable cavitation may occur. During the rarefactional part of the sound-wave cycle, the bubble radius increases to several times its original value. When the pressure gradient changes, the bubble collapses adiabatically and temperatures are attained at which free radicals are formed. When these free radicals recombine, light is emitted. This emission of light is known as sonoluminescence. It has been suggested that sonoluminescence occurs only in the presence of standing waves. This paper presents results of observations in aqueous systems, of the spatial distribution of sonoluminescence, as viewed by a high-gain image intensifier, when using different reflecting surfaces to establish ultrasound fields with different standing-wave ratios. For the experiments described, a physiotherapeutic ultrasound generator (Therasonic 1030, Electro-Medical Supplies), operating at 1 MHz in continuous-wave mode, was used. Measurements of the acoustic pressure variations on the axes of the sound fields were made using a needle hydrophone, and the resulting patterns of maxima and minima were compared with photographs of the spatial distributions of the light output from the image intensifier. The densities of the negatives were recorded using a microdensitometer (Joyce-Loebl). This enabled quantitative values of light intensity to be compared with standing-wave ratios. It was found that bands of maximum light corresponded extremely well with regions of maximum pressure variation as recorded by the hydrophone, demonstrating convincingly that sonoluminescence originates at pressure antinodes in a sound-wave field. Very little light was produced by progressive-wave fields. The extent to which these results support the hypothesis that in aqueous media sonoluminescence is produced only by standing waves is discussed. The results of experiments at room temperature and at 37°C were used to obtain information on the effect of temperature on sonoluminescence.

## A STUDY OF ULTRASONIC PULSE-ECHO BEAM-HARDENING USING TISSUE-MIMICKING TEST OBJECTS

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The use of broad-band pulses in diagnostic ultrasound is imperative in order to ensure optimum resolution. However, because of the strong frequency dependence of attenuation coefficient, $\alpha$, of soft tissue ($\alpha \propto f^{1.2}$), there is a preferential absorption of the higher-frequency components of the pulse and hence a "beam-hardening" effect. The result is that the effective frequency of the pulse decreases with increasing depth. The use of tissue-mimicking materials, such as in the Cardiff Test System, to measure scanner dynamic range relies upon the assumption that the effective frequency is depth-dependent. Observations on several scanners where observed dynamic range is depth-dependent suggests that this beam-hardening may be a real problem. We have attempted to quantify the beam-hardening effect using varying path lengths in tissue-mimicking material and to relate these measurements to the apparent change in dynamic range with depth. The results obtained from several commercial scanners show the important influence of the low-frequency components and the lack of correlation between dynamic range, centre frequency, penetration and resolution.

## COMPUTER-CONTROLLED GAIN COMPENSATION IN ULTRASONIC IMAGING

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A simple form of automatic gain compensation has been shown to be of value in obstetric and abdominal ultrasound (Pye et al, 1983, 1985). A new computer-controlled gain-compensation system has been developed which can apply a different gain function to each beam direction in the image. For gain calculations, each beam direction is divided into 3 mm range intervals. Several algorithms have been developed for generating TGC functions. These are described and the results of using them clinically and with ultrasound test objects are presented.

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## APPLICATIONS OF A NEW VISUALISATION SYSTEM

J. Szilard

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A new real-time scanner is to be based on a multi-element probe arrangement of new design and using new technology. As a result, scanning can be focused in a coaxial plane (B-scan type) or in an orthographic plane (C-scan type), or in any plane between Good resolution is possible axially and in the two dimensions perpendicular to the axis of propagation. Even a volume may be scanned to produce a pseudo three-dimensional image. Scanning any plane can be accomplished in a fraction of a second, so the operation is practically real-time. Volume scanning of course takes longer, a few seconds, which is still not unacceptably long Because of this extreme versatility it will be called Universal Imager, or U-scanner for short. As work is still in a very early stage and commercial confidentiality might be involved, only an outline of the system is given. Instead of technical details, the emphasis is on discussing potential clinical applications and of how the requirements of potential users can best be satisfied.

## A NON-LINEAR SPACE-VARYING TECHNIQUE TO REDUCE SPECKLE IN ULTRASONIC IMAGES

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Ultrasonic scans of soft tissues exhibit a characteristic granular pattern, known as speckle, which is an interference effect caused by the scattering of ultrasonic waves from microscopic tissue inhomogeneities. While the mean grey-scale level of speckle provides information about the tissue echogenicity, the spatial variation of speckle (texture) depends heavily on the imaging parameters and bears little resemblance to the actual tissue microstructure. Speckle is one of the main sources of degradation in ultrasonic imaging because it reduces the visibility of small structures and limits the detection of low-contrast lesions within the parenchyma. In order to suppress speckle by means of digital signal processing, a new technique called the adaptive weighted median filter has been developed The technique is based on median-type filters which have been used as an alternative to linear filters for noise smoothing because of their excellent edge-preserving properties By adjusting the weight coefficients and, consequently, the smoothing characteristics of the adaptive weighted median filter according to the local statistics around each point of the image, it is possible to suppress noise while edges and other important features are preserved. Application of the filter to several abdominal ultrasonic scans has shown that processing improves the detectability of subtle grey-scale variations within the parenchyma without affecting the sharpness and structural information of the original image.

## ANALYSIS AND FILTERING OF ULTRASONIC SPECKLE

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Papers at the two previous annual meetings of The British Medical Ultrasound Society have introduced the concept of a post-processing technique which uses local image texture features to recognise and remove speckle from echograms, and have illustrated its use and limitations in an early clinical trial (Bamber & Daft, 1985; Bamber & Cosgrove, 1986). The early clinical experience demonstrated that it will probably be necessary to use spatially variant reference features, and to use both first- and second-order texture features, to be sure that no useful information is lost from the processed images. Because of the large number of variables which must be studied when attempting to develop multivariate speckle filters, it has been necessary to construct a flexible software environment, within which a particular design of filter is implemented as a sequence of discrete (global) operations on whole images. Once a sequence of operations has been defined (which defines a filtering algorithm) it may be stored as a file and later recalled for execution using any desired input image. Such a file is, essentially, a very high-level program which is very easily altered to create a new filtering algorithm using perhaps a different number of, or alternative, texture features. This approach has the added advantage of producing filtering algorithms which are already in a form suitable for implementation on a parallel computer (of the single-instruction multiple-data kind) and, hence, possibly achieving processing speeds approaching real-time. It has also been necessary to return to a more fundamental study of the properties of speckle and texture in echographic images to consider, amongst other things, whether there are advantages in working with the radio-frequency signal rather than the demodulated video signal. Thus a second part of the presentation concerns an analysis of texture features of magnitude and phase in images chosen to represent both resolved and unresolved scattering structures. Filtering algorithms which make use of local phase properties of echo images are also discussed.

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# Obstetric ultrasound

**Chairman: C. R. Whitfield**
**Co-chairman: K. Cietak**

The use of Doppler in the assessment of fetal well-being, by J B. Wilsdon, K. Martin, H. Cameron and T. A Whittingham
The role of Doppler ultrasound waveform in the management of pregnancies complicated by intrauterine growth retardation, by N. G. Haddad, S. C Chambers, F. D. Johnstone, P. Hoskins, B. B. Muir and W. N. McDicken
A new approach to the analysis of fetal doppler-shift waveforms, by P. Stone and R. Skidmore
Doppler assessment of the fetal and uteroplacental circulations in normal and complicated pregnancies, by W. Al-Ghazali, L. D. Allan and M G Chapman
Routine assessment of fetal cardiac anatomy by the non-specialist: survey of factors affecting image quality, by D C. Crawford, S Kaur-Chita and L. D. Allan
The relative roles of clinical examination and ultrasound in the assessment of first trimester bleeding, by M R. Gowland, H. H. Awad and S Fielding
Receiver operating characteristic curves in obstetric ultrasound, by N J Dudley

## THE USE OF DOPPLER IN THE ASSESSMENT OF FETAL WELL-BEING

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Patients drawn from the Antenatal Clinic and antenatal wards were examined using Doppler ultrasound at varying times between 20 weeks' gestation and term. On each occasion, umbilical artery and bilateral uterine arcuate waveforms were obtained and in some instances waveforms directly from the placental bed The information was acquired using an ultrasonic duplex system consisting of a mechanical sector scanner interfaced to a range-gated Doppler unit and frequency analyser. Images and waveforms were obtained using the same transducer On occasions a continuous-wave Doppler probe was used Doppler signals were recorded and later analysed using a Doptek frequency analyser interfaced to a BBC microcomputer. For each waveform a maximum frequency envelope for up to 15 cycles was extracted and the *A/B* ratio calculated by the computer together with the standard deviation To date 145 patients have been examined. Overall there was agreement between the Doppler prediction and the clinical outcome, both normal and abnormal, in 121 There were 17 false positive and seven false negative results. An initial assessment of reproducibility of the waveforms between different operators is given.

## THE ROLE OF DOPPLER ULTRASOUND WAVEFORM IN THE MANAGEMENT OF PREGNANCIES COMPLICATED BY INTRAUTERINE GROWTH RETARDATION

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Intrauterine growth retardation (IUGR) has well recognised implications in obstetrics. It has been estimated that it can contribute to about 20% of the perinatal mortality rate At present, most pregnancies are screened for the detection of IUGR by serial symphysial fundal height measurements and diagnosis of the condition is made by ultrasound scan measurements of various fetal parameters Once antenatal diagnosis is made, extensive evaluation by serial ultrasound scans and intensive fetal surveillance is usually done to assure fetal well-being However, only a proportion of these small babies are compromised. We postulate that Doppler ultrasound waveforms obtained from the umbilical and arcuate arteries might help to predict which fetus is compromised and thus in need of intensive fetal surveillance. We are studying a population of patients who are clinically diagnosed as "suspected small for gestational age", confirmed by ultrasound scan measurements. All these patients have otherwise apparently uncomplicated pregnancies (no hypertension, renal disease, antepartum haemorrhage, etc.) At the time of writing over 50 patients have delivered and around 70 patients have been studied We present data firstly answering whether Doppler ultrasound waveform is a better predictor of growth retardation than other techniques and secondly, within the growth-retarded population, whether flow velocity waveform analysis is a more reliable indicator of serious fetal compromise.

## A NEW APPROACH TO THE ANALYSIS OF FETAL DOPPLER-SHIFT WAVEFORMS

P. Stone and R. Skidmore

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During the last few years, Doppler ultrasound has been used to study blood flow and velocity changes in the developing fetus, with the aim of improving the assessment of fetal welfare The difficulty in obtaining accurate estimates of volume flow has led many workers to consider only the blood flow velocity time patterns expressed in terms of simple indices such as pulsatility index However, the use of such simple indices may not have the ability to discriminate the subtle changes that may differentiate between health and disease. The use of more sophisticated waveform analysis techniques have been shown to be beneficial in describing the changes that occur in peripheral vascular disease These techniques involve describing the complete blood velocity time waveform in the frequency domain in terms of its Laplace transform which is of the form.

$$V(S) = \frac{1+AS^2}{1+BS+CS^2+DS^3}$$

where $S = jw$ Using these more powerful methods of pattern recognition, we have studied the changing velocity patterns obtained from the fetal aorta and umbilical arteries with advancing gestation. Preliminary results suggest that subtle changes do occur in the fetal aortic waveform shape that can be detected late in the second trimester. The methodology and initial results are presented.

# *Proceedings of The British Medical Ultrasound Society*

## DOPPLER ASSESSMENT OF THE FETAL AND UTEROPLACENTAL CIRCULATIONS IN NORMAL AND COMPLICATED PREGNANCIES

W. Al-Ghazali, L. D. Allan, M. G. Chapman

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The normal range for blood velocity waveforms, in both the umbilical and uterine arteries, and for combined cardiac output has been established in normal pregnancies In the umbilical and uterine arteries there are high diastolic flow velocities, reflecting low placental resistance Placental resistance falls as pregnancy advances, as evidenced by a decreasing systolic · diastolic ratio in these vessels. Although combined cardiac output (the sum of left and right ventricular volume flow) shows wide individual and diurnal variation, centile graphs for volume flow/kg body weight throughout pregnancy have been derived. Flow falls per kg from about 450 $cm^3/min$ at 26 weeks' gestation to about 300 $cm^3/min$ by term.

A series of 39 complicated pregnancies were studied by Doppler evaluation of umbilical, uterine and intracardiac velocities. There were 19 cases of suspected intrauterine growth retardation On serial examination seven cases continued to have normal flow velocities in all sites; none of these cases had an abnormal course during or after delivery. In the remaining 12 cases, there was evidence of increasing placental resistance as gestation advanced, a reversal of the normal trend. In all 12, fetal distress developed during labour, necessitating intervention. There were two still births in this group; the remaining 10 infants all required neonatal intensive care. Twenty cases of maternal hypertension were studied. There were abnormal uterine artery flow velocity waveforms in six cases; four also had abnormal umbilical artery traces. These four all had a bad outcome of pregnancy. In those cases with normal blood flows the outcome was good. Of the whole series of 39 cases only three showed abnormal combined cardiac output. Two of these cases resulted in stillbirths; one survived after a prolonged and stormy post-natal course.

We conclude that serial Doppler evaluation can have a useful role in the management of complicated pregnancies, in the timing of delivery and prediction of fetal distress during labour. Fetal combined cardiac output appears to be well maintained until very late in the course of fetal compromise but low values are a very poor prognostic sign.

## ROUTINE ASSESSMENT OF FETAL CARDIAC ANATOMY BY THE NON-SPECIALIST: SURVEY OF FACTORS AFFECTING IMAGE QUALITY

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and Lindsey D. Allan

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Congenital heart disease is now the most common congenital anomaly in the newborn. Severe cardiac defects are usually associated with a very poor long-term prognosis, but most are detectable by ultrasound using the "four chamber view" (Allan et al, 1986). To encourage all ultrasound units to examine the fetal cardiac anatomy using this view, a training programme involving "site visits" has been in progress for a year A survey to assess the success rate of cardiac scanning during routine antenatal scan sessions has been carried out in collaboration with many ultrasound departments who have received "hands on" tuition. Each participating department recorded details of all antenatal scans performed between 12 weeks' gestation and term, and noted whether a four chamber view of the fetal heart could be obtained Analysis of the results of including cardiac scanning in over 2000 antenatal ultrasound examinations is presented Factors which affect the quality of the ultrasound image include gestational age, maternal obesity, fetal lie and the ultrasound imaging equipment used for the examination. The relative importance of these factors is evaluated. The features of ultrasound imaging equipment which enhance the visualisation of fetal cardiac anatomy are demonstrated by a video-tape presentation.

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## THE RELATIVE ROLES OF CLINICAL EXAMINATION AND ULTRASOUND IN THE ASSESSMENT OF FIRST TRIMESTER BLEEDING

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At our centre it is policy to scan all admissions to the gynaecological wards presenting with bleeding in the first trimester of pregnancy. Because of recent controversy about "routine" scanning, a retrospective study was carried out on 100 consecutive patients who presented in this way. The relative value of clinical examinations (including pregnancy tests) and ultrasound examination was assessed in order to determine whether this policy examination is justified.

## RECEIVER OPERATING CHARACTERISTIC CURVES IN OBSTETRIC ULTRASOUND

N. J. Dudley

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Receiver operating characteristic (ROC) curves have been used for many years in the evaluation of imaging-system performance. Recently their use in obstetrics has been suggested, with particular reference to the evaluation of biochemical and biophysical tests This paper demonstrates how their use can be extended into the field of obstetric ultrasound.

An ROC curve is a graph of the conditional probability of true positive responses versus the conditional probability of false positive responses of an observer in a detection experiment, and is a way of representing detection performance which, unlike sensitivity and specificity, takes into account variability of the criterion level These curves provide a simple yet meaningful method for comparing the performance of different measured parameters and for determining optimum "cut-off" points for their use in clinical diagnosis Examples of the use of ROC curves in the particular case of the detection of intrauterine growth retardation (IUGR) are presented, showing that many different combinations of fetal dimensions can be quickly compared. This exercise demonstrates that combining the commonly used measurement of fetal abdominal circumference with other parameters reduces its effectiveness, but also that in using this parameter further consideration should be given to its interpretation. Some ROC curves are shown which demonstrate the optimum gestation for scans to detect IUGR, and the optimum "cut-off" levels for abdominal circumference. In conclusion, the ROC curve provides a visually meaningful alternative to more complicated statistical analyses whose results are often difficult to interpret in terms of clinical usefulness.

# Paediatric ultrasound

**Chairman: N. Rutter**
**Co-chairman: K. Shah**

Patterns of brain ischaemia in newborn infants, by S. Sinha, J. Davies, D. Sims and M. Chiswick
Echo-dense periventricular leucomalacia, by D. I. Rushton, P. R. Preston, G. M. Durbin and M. E. I. Morgan
Ultrasonic diagnosis and monitoring of rickets in immature infants, by D. K. Nassir, N. McIntosh, A. Lyon, V. Newey and M. Doran
Diagnosis and treatment of intussusception using ultrasound, by G. M. Steiner
Liver Doppler in biliary atresia, by H. B. Meire and S. Coates

## PATTERNS OF BRAIN ISCHAEMIA IN NEWBORN INFANTS

Sunhil Sinha, Jackie Davies, Douglas Sims and Malcolm Chiswick

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Introduction of high-resolution probes and frequent ultrasound scanning allows not only the diagnosis of ischaemic brain lesions early in the neonatal period but also the exploration of their prognostic significance. Moreover, it is possible to time their onset with reasonable accuracy and study their clinical correlates more easily than in the past. We did serial scans on 281 babies (age $\leqslant$ 32 weeks' gestation) admitted consecutively to our unit over 20 months. Changes consistent with brain ischaemia were found in 42 babies (14.9%). In nine (21.4%) the ischaemic changes were present at birth (median time of diagnosis 30 min) as compared with the rest, where the time of onset of these lesions varied from 4 to 70 (median 7) days ($p < 0.01$). Comparison of these two sets of babies with early- and late-onset ischaemic lesions showed that they were far from homogeneous. The distribution of ischaemic lesions in the early-onset group was always in periventricular white matter, whereas in the late-onset group cortical (diffuse and focal) and subcortical lesions were also seen. Significant differences were also noted in their birth history, early neonatal course, incidence of associated periventricular haemorrhage ($p < 0.05$) and mortality ($p < 0.01$). The only feature common to both groups was a very high incidence of neurodevelopmental disability. At least two-thirds of survivors who had evidence of brain ischaemia on ultrasound scans have signs of cerebral palsy on follow-up at 10–18 months of age. Our findings indicate that brain ischaemia in pre-term infants is a more potent cause of perinatal brain damage than periventricular haemorrhage and represents a continuum involving pre-natal, intrapartum and neonatal events.

## ECHO-DENSE PERIVENTRICULAR LEUCOMALACIA

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The periventricular regions of the brain of the pre-term neonate are known to be particularly susceptible to circulatory disturbances. Two major groups of lesions are recognised, subependymal haemorrhage simplistically related to hyperperfusion of the brain and periventricular leucomalacia (PVL) related to hypoperfusion. There is growing evidence from follow-up studies that the prognosis of the former disorder is good whereas it is frequently very poor with the latter. Both groups of lesions may be associated with intraventricular haemorrhage. This paper discusses the ultrasound diagnosis of PVL in the early echo-dense phase and comparisons between ultrasound and post-mortem appearances are made. Follow-up material is presented.

## ULTRASONIC DIAGNOSIS AND MONITORING OF RICKETS IN IMMATURE INFANTS

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Extremely immature infants commonly develop rickets of prematurity. This seems to be due to mineral deficiency rather than a problem with vitamin-D intake or metabolism. As a part of a research programme at St George's Hospital, to develop a reliable, easy-to-operate, non-invasive, low-risk technique for diagnosis and monitoring of rickets in immature infants, we are measuring the velocity and attenuation coefficient of ultrasound as a function of frequency in infants' bones. These measurements can provide useful information about the density of the bone as well as the structure of spongy cancellous bone. In this study a wide-band ultrasonic pulse (0.5–5.0 MHz) is transmitted through the wrist. The received signal is amplified and isolated by a receiving time gate. It is then digitised by a 48 MHz 6-bit analog-to-digital converter, before being fed into a microcomputer where the frequency spectrum of the pulse is computed. A reference pulse propagated through the same thickness of water is also fed into the computer. The velocity in the wrist is computed from the time difference between reception of these two pulses. The attenuation coefficient as a function of frequency is computed from the intensity differences between the two spectra. This paper reports on the study of velocity and attenuation coefficient in a group of 15 normal mature babies, together with longitudinal studies of 15 premature infants. The results are discussed and compared with the results of a technique of dual-energy X-ray densitometry which is being developed in our department.

## DIAGNOSIS AND TREATMENT OF INTUSSUSCEPTION USING ULTRASOUND

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Intussusception is a well recognised cause of an acute abdomen in the infant. Although the ultrasound appearances of intussusception are non-specific, they are reliable in the correct clinical context. They have to be differentiated from faeces, kidney in abnormal position, inflammatory bowel disease and neoplasm. Reduction of the intussusception can successfully be controlled using ultrasound. The progress of the reduction is easily followed and success is signalled by a sudden deflation of the bowel and gush of fluid. Equally important, lack of success is also evident.

### LIVER DOPPLER IN BILIARY ATRESIA

H. B. Meire and S. Coates

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Nearly 100 children are born in the United Kingdom each year with biliary atresia The Kasai procedure (porto-enterostomy) is usually the only form of surgical therapy possible. In the absence of adequate biliary drainage, progressive secondary biliary cirrhosis occurs. Doppler ultrasound studies of the blood-flow pattern in the portal veins, hepatic artery and hepatic veins is being used to help assess the degree of liver change and to monitor post-operative patients. The changes seen to date are very different from those observed in most forms of progressive adult liver disease. We present and discuss preliminary findings.

## Gynaecological ultrasound

**Chairman: C. R. Whitfield**
**Co-chairman: K. Cietak**

A comparison of abdominal mechanical sector ultrasound with vaginal mechanical sector ultrasound in monitoring follicular growth and development during natural and clomid cycles, by R. K. Goswamy, G. Williams, C. Howles, M. Macnamee, R. G Edwards and P. C. Steptoe

Can ultrasound alone determine normality and maturity of ovarian follicles? by E. J Thomas and E. A. Lenton

Ultrasound uterine measurement versus plasma progesterone levels as predictors of conception cycles in *in-vitro* fertilisation patients, by R. K Goswamy, G. Williams, C. Howles, M Macnamee, P. C Steptoe and R. G Edwards

Ultrasound evaluation of the endometrium and associated ovulatory changes endometrial studies in the assessment of early gestation and the diagnosis of ectopic pregnancy, by B. Smith, I. Craft, C. Keegan, J Evans and E. Fincham

Pelvic ultrasound findings in women with chronic pelvic pain. correlation with laparoscopy and venography, by J Adams, R Beard, P Reginald and S Franks

The use of transrectal ultrasonography in the evaluation of and treatment planning for pelvic malignancy, by J. M. Rodriguez, M Halliwell, D. Coules, S. Hilton, E. C. Whipp and H. Eckert

Doppler ultrasound of the uterine artery and uterus in invasive mole and choriocarcinoma, by M. G Long, J. E Boultbee, R. H. J. Begent and K. D. Bagshawe

### A COMPARISON OF ABDOMINAL MECHANICAL SECTOR ULTRASOUND WITH VAGINAL MECHANICAL SECTOR ULTRASOUND IN MONITORING FOLLICULAR GROWTH AND DEVELOPMENT DURING NATURAL AND CLOMID CYCLES

R. K. Goswamy, G. Williams, G. Howles,
M. Macnamee, R. G. Edwards and P C. Steptoe

*Bourn Hall Clinic, Bourn, Cambridge*

Abdominal ultrasound has been used extensively for monitoring the ovarian cycle in infertility practice since Hackeloer and Robinson (1978) described its use. The patient requires a full bladder and abdominal scanning, obesity and ovarian position can make adequate visualisation of follicles difficult Vaginal ultrasound does not require a full bladder and image quality is markedly improved, thus overcoming the problems experienced with abdominal ultrasound. All patients were scanned per abdomen and then scanned again the same day, vaginally by an observer unaware of the abdominal findings The main follicular diameter for each follicle was recorded. Preliminary data indicate a good correlation between vaginal and abdominal follicular diameters ($r = 0.93$). The results presented include a detailed analysis of the ability to detect follicles and visualise both ovaries and a comparison of: follicular diameter measurements; correlations between follicular size, oestrogen levels and LH levels, and patient acceptability of both methods. Vaginal ultrasonography is superior to abdominal imaging in infertility practice and most patients find. this an acceptable method of monitoring follicular growth.

### REFERENCE

HACKELOER, D. J & ROBINSON, H. B., 1978. Ultrasound examination of the growing ovarian follicle *Geburtshilfe und Frauenheilkunde, 38,* 163–168.

### CAN ULTRASOUND ALONE DETERMINE NORMALITY AND MATURITY OF OVARIAN FOLLICLES?

E. J. Thomas and E. A. Lenton

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The use of ultrasound alone to determine follicular normality and maturity contains two main sources of error The first is the reproducibility of the measurements with different observers The second is the capacity for ultrasonic observations to determine abnormal follicular growth accurately without synchronous endocrine data. The observer variability in three ultrasonographers was assessed by 10 replicate blind measurements of the diameter of five separate follicles. The maximum intra- and inter-observer coefficients of variation were 7 9% and 8.8% respectively Thirty-one women attempting to conceive were recruited to a study in which one menstrual cycle was intensively investigated by daily ultrasonic delineation of follicular growth combined with synchronous plasma, luteinising hormone and oestradiol estimations. Fourteen women spontaneously conceived during the study cycle and were defined as normal and compared with the 17 non-conception cycles. There was no significant difference in the mean maximal follicular volume in the conception (3.3 ml) and in the non-conception cycles (2.6 ml). The variability in growth patterns was larger in the non-conception cycles and was a reflection of the following follicular abnormalities. one premature rupture, one delayed rupture and two late growths. None of these abnormalities could have been prospectively categorised without synchronous endocrine data, especially the timing of the LH surge It is concluded that the ultrasonic measurement of follicular diameter is reproducible and consistent between observers However, while it is useful for determining follicular growth and rupture, the prospective assessment of normality and maturity can be made only with parallel hormone data

## ULTRASOUND UTERINE MEASUREMENT VERSUS PLASMA PROGESTERONE LEVELS AS PREDICTORS OF CONCEPTION CYCLES IN *IN-VITRO* FERTILISATION PATIENTS

R K. Goswamy, G. Williams, C. Howles, M. Macnamee, P. C. Steptoe and R. G. Edwards

*Bourn Hall Clinic, Bourn, Cambridge*

Uterine area has been measured by several workers since it was first described by Adams et al as a possible predictor of conception cycles Encouraged by this work we set up a prospective study to measure uterine areas in all patients attending for *in-vitro* fertilisation (IVF) treatment at Bourn Hall. More than 400 patients have been scanned during their follicular phase scans and again on Day 2 and Day 6 (post-oocyte recovery) Plasma progesterone levels were measured on Days 2, 6 and 12 (post-oocyte recovery) and comparisons were then made to check the predictive value of each of these measurements Preliminary results indicate no difference in mean progesterone levels nor in uterine size on Days 2 and 6 between pregnant and non-pregnant patients. However, results on Day 12 post-oocyte recovery indicate that progesterone is not only a predictor of conception cycles but that it can also predict ectopic pregnancies There was a trend towards an increased rate of uterine growth in conception cycles and we would conclude that uterine area measurement is of no significant predictive value in IVF patients. More sensitive measures are required and investigations are currently being carried out to look for these

## ULTRASOUND EVALUATION OF THE ENDOMETRIUM AND ASSOCIATED OVULATORY CHANGES: ENDOMETRIAL STUDIES IN THE ASSESSMENT OF EARLY GESTATION AND THE DIAGNOSIS OF ECTOPIC PREGNANCY

B. Smith, I. Craft, C. Keegan, J. Evans and E. Fincham

*Department of In-Vitro Fertilisation and Fertility Studies, Humana Hospital Wellington, London*

Advances in instrument performance relating particularly to improved sensitivity and grey-scale capability has enabled detailed ultrasonic study of the endometrium. The endometrium is clearly delineated in most cases, certainly in the absence of pelvic pathology and with a normal anteverted uterus Two aspects of the endometrium appear to change progressively during a natural or stimulated ovulatory cycle, namely its thickness and reflectivity or grey-scale appearances. A simple grading system (A to D) relating to textural changes within the endometrium has been described by Smith et al (1984) This has resulted in greater appreciation of endometrial development and subsequent degeneration through the pre-ovulatory, peri-ovulatory and luteal phases of the ovulatory cycle. The above paper was based on a prospective study, carried out in 1982 and 1983, of 297 patients following the initial observations of endometrial appearance in more than 1000 patients undergoing preparation for *in-vitro* fertilisation Multiple ovulation was induced by the administration of clomiphene citrate and HMG. Group 1 consisted of 189 patients in whom 2000 IU HCG was administered when the leading follicle reached a mean diameter of 18 mm Group 2 consisted of 108 patients in whom an assessment of the endometrial response was made and used as an additional parameter for HCG administration 2000 IU was given when the mean diameter of the leading follicle was greater than 15 mm in the presence of an endometrial response defined as "C" grade and of at least 5 mm total thickness The oocyte retrieval rate for both groups was similar (90% and 87%) as was the mean number of oocytes collected per patient (3.9 and 4.0) However, there was a significant increase in the fertilisation rate (60% to 83%) and 65% of patients in Group 1 undergoing replacement of at least one embryo compared with 91% in Group 2. The significant increase in fertilisation rate with a drastically reduced pre-egg collection ovulation rate tends to confirm a more appropriately timed oocyte collection and a greater appreciation of the quality of an ovulatory response using the above endometrial parameters The endometrium develops further following ovulation, showing an increase in thickness and rapid textural changes, becoming much brighter in appearance than the myometrium During the latter half of the luteal phase, however, there are characteristic degenerative changes noted ultrasonically, again in terms of reduced thickness as well as textural variations However, rapid proliferation occurs following conception which has proved to be of good prognostic value in the assessment of very early gestations Similarly, endometrial studies as such have become essential in the diagnosis of ectopic pregnancies. Our experiences and techniques used in scanning a large number of tubal, ovarian and cornual pregnancies over recent years are described

### REFERENCE

SMITH et al, 1984. Ultrasonic assessment of endometrial changes in stimulated cycles in an *in-vitro* fertilisation and embryo transfer program. *Journal of In Vitro Fertilisation and Embryo Transfer.*

## PELVIC ULTRASOUND FINDINGS IN WOMEN WITH CHRONIC PELVIC PAIN: CORRELATION WITH LAPAROSCOPY AND VENOGRAPHY

Judith Adams, R. Beard, P. Reginald and S Franks

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Patients with chronic pelvic pain typically have pelvic varicosities, demonstrated by venography, but no other obvious abnormalities of the pelvic organs Pelvic ultrasound scans were performed in 73 women with chronic pelvic pain and the findings compared with those from laparoscopy (in 46 women) and pelvic venography (41) All scans were performed by the same observer (J.A.) who was blind to the results of other investigations The uterus, endometrium and ovaries were measured and pelvic pathology noted, including the presence of pelvic varicosities. Polycystic ovaries (PCOs) were found in 44 of 73 women (60%). Polycystic ovaries were confirmed in 39 of 46 women who also underwent laparoscopy, giving an 85% correlation with the ultrasound findings The ovarian volume was significantly greater ($p < 0.001$) in women with PCO ($12.9 \pm 3.8$ (SD)) than in normal women ($7.2 \pm 2.4$). The uterine cross-sectional area, assessed during the mid-follicular phase of the cycle, was similar in both groups (PCO 40.3 cm$^2 \pm 9$ (SD), non-PCO 36.2 cm$^2 \pm 9.2$) However, in both groups the uterine size was significantly larger than in a group of 15 normal women, matched for parity, who did not have pelvic pain (30.9 cm$^2 \pm 7.4$ (SD)). Varicosities were detected by venography in 33 of 41 patients and by ultrasound in 31 of these 33, so the sensitivity of ultrasound in the diagnosis of pelvic varicosities was very high (94%). This study demonstrates that pelvic ultrasound is a useful and accurate method of assessment of ovarian morphology and pelvic veins in women with pelvic pain and is a non-invasive alternative to venography in such patients.

### THE USE OF TRANSRECTAL ULTRASONOGRAPHY IN THE EVALUATION OF AND TREATMENT PLANNING FOR PELVIC MALIGNANCY

J. M. Rodriguez, M. Halliwell, D. Coules, S. Hilton, E. C. Whipp and E. Eckert

*Radiotherapy Centre, Bristol Royal Infirmary*

Advances in endoprobe technology have led to the application of transrectal ultrasound in the assessment of and treatment planning for pelvic malignancy. Experience in using such a technique in evaluating the stage and extent of gynaecological malignancies is described. Additionally, the technique has proven of value in visualising the central uterine tube and forniceal ovoids of a rigid remote $^{137}$Cs afterloading treatment system (Selectron) used in the intracavitary therapy of endometrial and cervical cancers. This finding is potentially important, in optimising the radiation dosimetry of such a system.

### DOPPLER ULTRASOUND OF THE UTERINE ARTERY AND UTERUS IN INVASIVE MOLE AND CHORIOCARCINOMA

M. G. Long, J. E. Boultbee, R. H. J. Begent and K. D Bagshawe

*Cancer Reserach Campaign Laboratories, Department of Medical Oncology and Department of Radiology, Charing Cross Hospital, London*

This study investigates the application of pulsed Doppler duplex ultrasound to assess blood flow through the pelvis in patients with invasive mole and choriocarcinoma. These are tumours of trophoblastic origin with a combined incidence of approximately one in 15 000 pregnancies and previous arteriographic evidence has shown that they are able to induce substantial vascular changes in and around the uterus. A method of scanning the uterus was established so that the returned frequency changes from the uterine arteries and myometrium could be reproducibly evaluated Twenty-six patients have been studied and the findings compared with those of a group of 22 normal subjects. It was found that the pulsatility index of the uterine artery and the Doppler status of the myometrium were significantly different from those of the normal group ($p < 0.001$ and $p < 0.01$), indicating an increase in blood flow and in 12 patients this abnormality persisted after biochemical remission of the disease. It can be concluded that pulsed Doppler ultrasound can be used to assess the haemodynamics of the uterine artery and myometrium and be used in the further study of these and other pelvic tumours. We would like to thank the Cancer Research Campaign for their support.

## Cardiological ultrasound

**Chairman: D. Gibson**
**Co-chairman: E. Silove**

An accurate non-geometric method of echocardiographic volume estimation, by J. M. Beattie, P. F. Wankling, J A. Newell and W. A. Littler

Pulsed Doppler ultrasound in the diagnosis of post-infarct ventricular septal defect, by M. G. Cheesman, R. John, J. Thomas and V. J. Redding

Post-operative assessment by Doppler ultrasonography after venous redirection operations for transposition of the great arteries, by S A. Qureshi, J. H. Dangel, R M Bini, R Arnold, R. McKay, J. L. Wilkinson and D I Hamilton

Detailed considerations for the measurement of $Q_p$, $Q_s$, and $Q_p/Q_s$ ratio in a paediatric population, by F. J. Soul, T. K Hames, G. R Sutherland and B R. Keeton

### AN ACCURATE NON-GEOMETRIC METHOD OF ECHOCARDIOGRAPHIC VOLUME ESTIMATION

J. M. Beattie, P. F. Wankling, J. A. Newell and W. A. Littler

*University of Birmingham and Department of Cardiovascular Medicine and Department of Medical Physics, Queen Elizabeth Hospital, Birmingham*

Conventional methods of echocardiographic ventricular volume estimation are inherently inaccurate, being based on simple geometric models which bear little resemblance to true morphology. A new method has been developed which appears to be devoid of such systematic errors. Based on Pappus' theorem, this approach uses a cylindrical co-ordinate system, the product of sectional area and centre of mass ($U$) of sequential short-axis scans being integrated with respect to the angle ($\phi$) through which the transducer is swept during their recording, $\int U d\phi$. This method was tested using computer-generated symmetric and asymmetric left-ventricular phantoms of known volume, simulating normal and abnormal ventricles For each left ventricle several short-axis scans were outlined to obtain their respective $U$ values. These short-axis scan samples were then aligned sequentially using internal cardiac landmarks common to an orthogonal long-axis plane, angle data ($\phi$) being derived by conventional geometry. Volume data from regions between short-axis scan samples were interpolated by outlining the long-axis image and measuring short-axis dimensions on radii projected from the transducer at 1° intervals. The square of the dimension versus angle curve was scaled to fit the previously obtained $U$ values and the corrected curve integrated to yield ventricular volume The results show this method to be robust. For example, symmetric and asymmetric ventricles of actual volume 151 ml and 157 ml respectively were estimated as 150 ml and 161 ml (error $\leqslant 3\%$). This degree of accuracy was maintained across a wide range of left-ventricular volumes and was independent of morphological variation This non-geometric approach therefore offers considerable advantages over those currently applied in clinical practice

### PULSED DOPPLER ULTRASOUND IN THE DIAGNOSIS OF POST-INFARCT VENTRICULAR SEPTAL DEFECT

M. G. Cheesman, R. John, J. Thomas and V J. Redding

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Nine consecutive patients with loud systolic murmurs developing during the course of acute myocardial infarction were referred. Seven patients were found to have acute ventricular septal defects, and two had severe mitral regurgitation. Pulsed Doppler ultrasound correctly diagnosed all seven patients with ventricular septal defects, and the site was identified with reasonable accuracy in six Two-dimensional echocardiography visualised the defect as an area of ragged myocardium in only five patients. Five patients proceeded to cardiac catheterisation for confirmation, but three were referred for surgery on Doppler and echocardiographic diagnosis alone One patient presented moribund and rapidly succumbed. One patient was noted to have a harsh systolic murmur 1 month after initially successful surgery; despite almost unchanged echocardiographic images, pulsed Doppler ultrasound confirmed partial patch dehiscence, and indicated which end of the patch was at fault Right-ventricular systolic pressure estimated from the velocity of the jet and the cuff arterial pressure was in good agreement with that obtained at catheterisation Pulsed Doppler ultrasound is a useful technique for the early non-invasive diagnosis of post-infarct ventricular septal defect and for post-operative follow-up.

### POST-OPERATIVE ASSESSMENT BY DOPPLER ULTRASONOGRAPHY AFTER VENOUS REDIRECTION OPERATIONS FOR TRANSPOSITION OF THE GREAT ARTERIES

S. A. Qureshi, Joanna H. Dangel, Roberta M. Bini, R. Arnold, Roxane McKay, J. L. Wilkinson and D. I. Hamilton

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Sixteen children (14 boys, two girls) underwent assessment by Doppler ultrasonography 1 week to 13 years (mean 32 months) after venous redirection by Mustard (11) or Senning (five) operations for transposition of the great arteries (TGA). The age at operation ranged from 3 to 38 (mean 11) months. All patients had simple TGA except one who had additional left-ventricular outflow tract obstruction (LVOTO). The peak blood flow velocities across the tricuspid valve (TV) were significantly higher than normal ($p < 0\ 05$) with mean $E$ wave of 87 (range 63–109) cm/s The mean ratio (SD) of peak $A$ to $E$ wave across TV was 0.61 (0.09) (range 0.41–0 74) Five (31%) of the children had mild tricuspid regurgitation No pulmonary venous obstruction was detected. The peak velocities across the mitral valve could not be evaluated in four patients and varied between 73 and 113 (mean 86) cm/s in the remainder. Satisfactory Doppler traces in the systemic venous atrium could be obtained in only 13 patients in whom the peak velocity ranged from 77 to 171 (mean 120) cm/s, with four patients having velocities $> 130$ cm/s. In two of these, cardiac catheterisation had confirmed the presence of baffle obstruction with gradients similar to those obtained by Doppler. The peak systolic blood flow velocities across the pulmonary valve were 87–185 (mean 115) cm/s, residual LVOTO being detected in one patient. Mild pulmonary regurgitation was found in two patients (12.5%). No aortic stenosis or regurgitation was seen In conclusion, Doppler ultrasound provides valuable information after venous redirection operations for TGA and may thus avoid the need for cardiac catheterisation However, difficulties may be encountered in the sampling of the systemic venous atrium to assess vena-caval baffle obstruction in a small number of patients.

### DETAILED CONSIDERATIONS FOR THE MEASUREMENT OF $Q_p$, $Q_s$ AND $Q_p/Q_s$ RATIO IN A PAEDIATRIC POPULATION

F. J. Soul, T. K. Hames, G. R. Sutherland and B. R. Keeton

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Previous workers who have attempted the measurement of absolute flow in the pulmonary artery ($Q_p$) and aorta ($Q_s$) using non-invasive duplex scanning, and hence the $Q_p/Q_s$ ratio, have made several assumptions which were examined in detail in this study. The intent was to judge their validity and provide accurate estimates of the errors involved in utilising specific protocols and equipment. A technical assessment of the equipment used (Toshiba and Hewlett Packard duplex scanners) including probe characteristics and flow rig simulation measurements are considered in a separate presentation. The two main parameters in estimating flow are the cross-sectional area of the vessel and the average mean velocity in the lumen throughout the cardiac cycle. In this study the former value was calculated from both M-mode and direct screen planimetric measurements, with the latter resulting from digitisation of the hard-copy spectrum analysis of the Doppler information Both pulsed Doppler (PD) and continuous wave (CW) ultrasound assessments were included in a measurement protocol developed to compare the flow values determined using: maximum (lumen width) and minimum sample volume sizes of the PD at the level of the aortic valve and in the main pulmonary artery, an assessment of the velocity profile across the width of the lumen of the pulmonary artery using multipositioning of the PD; and CW assessment of the aorta and pulmonary artery. This protocol was used in the assessment of two populations of paediatric patients, 20 clinically normal and 35 admitted to Southampton General Hospital for investigation. Using the 35 sets of data from the patient population inter- and intra-observer variability values have been calculated. In the latter population a catheter assessment of $Q_p/Q_s$ ratio in 12 cases was available for comparison with the non-invasive measurement.

*Proceedings of The British Medical Ultrasound Society*

# Vascular ultrasound

**Chairman: D. H. Evans**
**Co-chairman: M. Goldman**

Can surgeons reproducibly determine ankle vessel patency by ultrasound? by P I. Allen and M. Goldman
A comparison of duplex scanning, continuous-wave and pulsed Doppler ultrasound techniques in the measurement of aortic arch and great vessel velocity signals, by K. N. Humphries and T K. Hames
Femoral artery puncture: accurate localisation with Doppler ultrasound, by G. V. N Appleton, V. G. Langkamer and J. S. Harper
Abdominal inferior vena cava calibre, by A. W Robinson and P D. Birch

## CAN SURGEONS REPRODUCIBLY DETERMINE ANKLE VESSEL PATENCY BY ULTRASOUND?

P. I. M. Allen and M. Goldman

*East Birmingham Hospital*

Patency of distal lower limb vessels, necessary for successful distal limb salvage surgery, is commonly determined by arteriography. Recent reports suggest Doppler ultrasound in experienced hands may give more accurate information (Simms et al, 1984; Campbell et al, 1986) We have assessed the reproducibility of the technique, used at the bedside by non-specialist examiners and compared the results with angiography Twenty-four limbs were examined for palpable pulses by two surgeons. The limbs were then examined in six sites with Doppler ultrasound and systolic pressures measured wherever a signal was found There was clinical disagreement in five of 120 occasions (4%) involving the femoral artery once, the popliteal twice and dorsalis pedis twice. Ultrasound findings were concordant on 104 of 141 occasions (75%) when the limb was horizontal, rising to 81% when the limb was examined in dependency. Concordance between observers was not affected by any learning effect during the study, nor by the degree of ischaemia in the examined leg as reflected by the ankle-to-brachial pressure ratio. Pressure readings varied widely, agreeing within 10 mmHg on only 38% of occasions. Four patients did not have angiograms; of the remainder the film series failed to show the lower leg or ankle vessels adequately in nine. Findings agreed with ultrasound signals in only 37 of 60 instances (62%). On 19 occasions (32%), a signal was obtained, but the vessel was not outlined by contrast On four occasions, a vessel was seen to be patent on angiography, but there was no signal. In severely ischaemic limbs, ultrasound examination of the distal vessels in dependency is highly reproducible and superior to conventional angiography in the demonstration of patency, even when practised by inexperienced users. However, it cannot be relied upon for reproducible pressure measurement.

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SIMMS, M. H , HARDMAN, J. & SLANEY, G., 1984 The relevance of pre-bypass pedal arch assessment *British Journal of Surgery, 71*, 381.

## A COMPARISON OF DUPLEX SCANNING, CONTINUOUS-WAVE AND PULSED DOPPLER ULTRASOUND TECHNIQUES IN THE MEASUREMENT OF AORTIC ARCH AND GREAT VESSEL VELOCITY SIGNALS

K. N. Humphries and T. K. Hames

*Wessex Regional Medical Physics Department, Southampton*

There are now a number of studies outlining techniques for detecting and processing aortic arch velocity signals These have involved duplex scanning, continuous-wave and pulsed Doppler ultrasound techniques. There were two objectives to this study. One was to determine the optimum technique for detecting signals from the aortic arch, the innominate, the left common carotid and left subclavian arteries in order to assess the degree of constrictive arterial disease and thus complement the duplex assessment of the extracranial vasculature. The other was to determine the optimum technique for obtaining quantitive blood flow measurements from the aortic arch The equipment used was the Honeywell Ultra-Imager duplex scanner using special-application transducers of 2.25 MHz, 3.5 MHz and 5 MHz, suitable for suprasternum notch positioning, and the Vingmed SD-100 pulsed and continuous-wave Doppler system.The suprasternum notch approach was used for both pieces of equipment. Twenty-five controls within the age range 20–35 years were tested to determine the success rate of identification of these vessels. A further 25 patients with evidence of aortic arch, aortic valve or (L) ventricular abnormalities were also tested. The preliminary conclusions from these studies indicate that the duplex scanner is essential to identify the great vessels The aortic arch, the origin if the innominate and the innominate bifurcation were identified in all patients and controls tested. Identification of the origins of the (L) common carotid and (L) subclavian proved more difficult, but with experience these too were identified In order to identify the ascending aortic signal correctly using continuous-wave Doppler ultrasound, full knowledge of the innominate Doppler signature is necessary, but ideally a range-gated facility is used.

## FEMORAL ARTERY PUNCTURE ACCURATE LOCALISATION WITH DOPPLER ULTRASOUND

G. V. N. Appleton, V. G. Langkamer and J. S. Harper

*Departments of Surgery and Radiology, Musgrove Park Hospital, Taunton*

Blind femoral artery puncture with an angiographic needle is a commonly performed procedure. Although the artery is superficial it can be difficult to enter cleanly at the first attempt, especially in an obese patient. Inaccuracy may result in local haemorrhage, increased discomfort, and can considerably lengthen the investigation. Using a portable Doppler ultrasonic flowmeter the position and course of the underlying femoral artery can be determined. Immediately before arteriography the transducer is moved around the mid-inguinal region until the maximal audible arterial signal is attained. The skin is marked on either side of the transducer. This procedure is repeated at two further points along the line of the vessel. The position and direction of the femoral artery is, thus, outlined by two rows of marks The radiologist can confidently introduce his needle midway between the marks angled at 45° to the skin and directed along the exact course of the artery We have now used this method in 26 patients and have found it to be rapid, simple, non-invasive and helpful The complication of piercing the femoral artery at or below its bifurcation is avoided and the incidence of groin haematoma has been very low (< 4%). We strongly recommend the pre-angiographic localisation of the femoral artery using Doppler ultrasound

### ABDOMINAL INFERIOR VENA CAVA CALIBRE

A W. Robinson and P. D. Birch

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Excluding changes due to cardiac pulsation, there is a normal abdominal inferior vena cava (IVC) calibre variation during simple respiratory and muscular activity. The literature is instructive but reveals uncertainties A study was considered likely to be of interest and was undertaken. The upper abdominal antero-posterior IVC calibre and that of the portal vein at its origin were observed in 300 routine session cases with suspected pathology, but thought to be normal for our purpose Calibre variation was assessed in relation to obesity, during inspiration, on maintained inspiration, on Valsalva, and on straight leg raising during quiet breathing The usual pattern and significant variations were assessed, and explanations are postulated. Comment is offered on likely changes in intra-abdominal pressure between individuals, the effect of active inspiratory movement on intrathoracic pressure; the effect of glottic-held inspiration on intrathoracic pressure, and the possibly different effect of respiratory-muscle-held inspiration, the nature of the Valsalva manoeuvre, its variations, and the likely variable effect on IVC calibre; and the effect of straight leg raising during inspiration Comment is also made on those cases in which maintained inspiration produced both portal-vein distension and upper abdominal IVC antero-posterior diameter narrowing and the role, if any, of direct liver pressure upon the cava This was a simple study; other manoeuvres, for example simultaneous rectal and oesophageal pressures and assessments in different postures, would have been valuable. However, the exercise was instructive and it is presented in the hope that it is of interest.

## Specialist clinical applications

**Chairman: H. B. Meire**
**Co-chairman: D. Tudway**

Real-time breast echography: a Japanese approach, by E Ueno, E. Tohno, Y. Asaoka and K. Itoh
Sonomammography in benign breast disease, by P B. Guyer
Real-time ultrasound of the breast· a quantitative evaluation of diagnostic features, by E L. de Gonzalez, J C Bamber, D O. Cosgrove, J. A. McKinna and J Davey
The value of scrotal ultrasonography a clinical analysis, by R C Fowler
Ultrasound assessment of aspiration and tetracycline injection sclerotherapy for scrotal hydrocoele and epididymal cysts, by M. J Mitchell, W. J. G Murray, A. J Yates-Bell, J P Pryor, D A. Packham and H. B. Meire
Ultrasound in Peyronie's disease, by J L Isaacs, R Ewing and H. C Irving
Ultrasound-guided biopsy techniques, by P. G Lindgren
Ultrasound-guided renal allograft biopsy with the "Biopty" system, by C. S. Ubhi and H. C Irving
Clinical applications of sonically sensitive needles in fine-needle aspirations for cytology, by P. L Allan, T. Anderson and W. N. McDicken
Ultrasound imaging of the eye through the closed lid using a non-dedicated scanner, by J. A Fielding
Application of echography to thyroid screening: results of a preliminary study, by E. Ueno, E. Tohno, H Ushio, A. Yoshida, Y. Aiyoshi and S. Soeda
Value of ultrasound scanning in the parotid region, by A T. Irvine, J Browning-Smith, N. Stafford, P. R. Patel and G Walsh-Waring
The role of ultrasound in the assessment of unilateral parotid swelling, by J. V. Byrne and A. M Whyte

### REAL-TIME BREAST ECHOGRAPHY: A JAPANESE APPROACH

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The development of grey-scale sonography and high-frequency transducers have, in Japan, led to the recognition of breast echography (in the form of mechanical linear or arc scanners) as an adjuvant diagnostic tool on a par with film mammography. After the experience of using this method on some 4500 cases over a period of 7 years we decided, in November 1984, to try using a 7 5 MHz real-time mechanical sector scanner Since then we have performed real-time ultrasound examinations of the breasts of approximately 1300 women In this paper we review our diagnostic criteria and findings, concentrating on the real-time method We usually divide the echographic images of breast tumours into three types, according to the degree of ultrasonic attenuation attenuating, intermediate or accentuating These classes have relevance to the histological findings in that (as was shown by Kobayashi) connective-tissue content in breast cancer is a determining factor for ultrasound attenuation, and matured fibroadenoma also causes ultrasonic attenuation Thus, we have in previous papers proposed the diagnostic criteria in the Table

| | Attenuating | Intermediate | Accentuating |
|---|---|---|---|
| Malignant | Crab-like shape; halo (A = L) or (A < L) | Crab-like shape, heterogeneous internal echoes | Lobulated shape, heterogeneous internal echoes, large L/T ratio |
| Benign | Oval shape; no halo or (A > L) | Homogeneous internal echoes | Homogeneous internal echoes, small L/T ratio |

These criteria were devised using static breast echography Improved success was obtained when we added two new criteria resulting from the real-time method These were the elasticity assessed by manual compression and the response to a dynamic mobility test The poor elasticity and mobility of cancer can be seen easily using a real-time scanner.

As a result of the greater flexibility of real-time scanning our examination technique now also involves: (1) a sliding test to examine possible fixation to the muscle; (2) examination of the parasternal lymph node (due to Konishi), (3) a radial scanning sequence which is used when nipple discharge is present, so that dilated ducts may be detected more easily; and (4) guided aspiration cytology Mechanial scanners offered very fine static pictures. The real-time method has however, introduced additional diagnostic criteria, new techniques and a reduced examination time.

## SONOMAMMOGRAPHY IN BENIGN BREAST DISEASE

P. B. Guyer

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A detailed analysis of the first 2000 sonomammograms performed in this unit has revealed 451 patients with an ultrasound diagnosis of benign breast disease; in 121 of these there was histological confirmation of the diagnosis. In eight patients, biopsy revealed changes of diffuse benign disease when the ultrasound examinations were normal. There were four false negative ultrasound examinations when histology revealed diffuse infiltrating carcinoma, when ultrasound suggested diffuse benign disease, and there were 25 additional patients out of a total of 1077 ultrasound examinations in whom ultrasound incorrectly suggested malignancy the pathology in these patients was usually florid fibrocystic disease Ultrasound helped to avert surgery in 11 of 18 patients with diffuse disease scheduled for biopsy and changed the diagnosis from a benign condition to malignancy in three The place of pre-operative sonomammography in the X-ray-dense breast is outlined

## REAL-TIME ULTRASOUND OF THE BREAST: A QUANTITATIVE EVALUATION OF DIAGNOSTIC FEATURES

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Real-time ultrasound was introduced to the Early Diagnostic Unit at the Royal Marsden Hospital, London, a year ago as a complement to clinical and mammographic examination in the diagnosis of breast disease During this time a quantitative visual analysis was applied to the images of selected cases, with the dual objectives of aiding the learning experience and of quantitatively evaluating the relative value of various diagnostic criteria. Patients scheduled for excision biopsy or (in the case of presumed cysts) needle aspiration were selected for this study Scanning was performed before the biopsy. Histology or cytology was obtained in all cases, which included 25 with carcinoma. A Hitachi scanner with an 11 5 cm linear array at 5 MHz was used in direct contact with the skin. Both breasts were scanned with the patient supine (arms elevated) and slightly rotated away from the side being examined. Features from the images were classified visually and their degree assessed. The resulting score was entered into a computer for subsequent statistical analysis and comparison with the histological diagnosis The breasts were classified according to their glandular pattern using general features. When a lesion was demonstrated features specific to the mass were also evaluated, these included the regularity and smoothness of the borders, the heterogeneity of the echoes within, around and posterior to the lesion and mobility and compressibility We describe our early experience in using real-time ultrasound of the breast and the results of the quantitative feature analysis of the first 100 selected cases

## THE VALUE OF SCROTAL ULTRASONOGRAPHY: A CLINICAL ANALYSIS

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Three hundred and fifteen patients were referred for scrotal ultrasonography over a 2-year period. The great majority were referred from the Urology Department in this hospital, where they had been examined by experienced surgeons. This paper compares the clinical, ultrasonographic and, where possible, the pathological or operative findings. The results indicate the value of scrotal ultrasonography in clinical practice. Ultrasound achieved high accuracy (99%), sensitivity (96%), and specificity (99%). These results were clearly superior to clinical examination alone. Of particular importance was the demonstration of seven testicular tumours that were clinically, unsuspected or impalpable. Problem areas in accurate ultrasound diagnosis of scrotal disease are reviewed, and the need for scrotal ultrasonography as a first line of investigation is emphasised.

## ULTRASOUND ASSESSMENT OF ASPIRATION AND TETRACYCLINE INJECTION SCLEROTHERAPY FOR SCROTAL HYDROCOELE AND EPIDIDYMAL CYSTS

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There has been recent interest in aspiration and tetracycline sclerotherapy as an alternative to surgery in the management of scrotal hydrocoele and epididymal cysts (Bodker et al, 1985) In this prospective study, ultrasound was used to assess this treatment objectively in 20 patients (mean age 66 years) with unilateral symptomatic fluid scrotal swellings. Seventeen had hydrocoeles and three had epididymal cysts. In the hydrocoele group, the swelling had been present for a mean period of 31 (range 6–120) months. At the patient's initial visit a scrotal ultrasound examination was performed and the volume of fluid present calculated using a standard formula for calculating the volume for an ellipsoid. The volume of the testis was subtracted from the total volume of the hemiscrotum to give the volume of fluid in the hydrocoele or epididymal cysts. The mean volume of hydrocoele fluid before aspiration was 282 (range 65–1017) ml After aspiration of fluid and injection of 500 mg of tetracycline hydrochloride, serial ultrasound examinations were carried out after 2 weeks, and then approximately at 3-monthly intervals, to assess the volume of any residual fluid and to demonstrate morphological changes in the scrotum. The correlation coefficient of ultrasound estimation of fluid volume and aspiration volume of fluid is 0.977 Fifteen (88%) of the patients with hydrocoeles were successfully treated (residual volume less than 15 ml) with a mean follow-up of 9.5 (range 3–14) months The formation of septa with loculation of fluid was demonstrated in four patients Only one of the patients with epididymal cysts was successfully treated and in one other patient an abcess requiring surgical drainage was demonstrated Ultrasound has been helpful in objectively assessing the efficacy of aspiration and injection sclerotherapy, which can be recommended for the treatment of simple hydrocoele

## REFERENCE

BODKER, A, et al, 1985 *British Journal of Urology, 57,* 192–193

## ULTRASOUND IN PEYRONIE'S DISEASE

J. L. Isaacs, R. Ewing and H. C. Irving

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In Peyronie's disease, fibrous plaques in the shaft of the penis may result in erection with curvature of the penis which can be painful. Attempts at treatment of the condition vary from local surgical procedures to systemic drug therapy (*e g.* Potaba, Glenwood), but objective assessment of the effectiveness of the various remedies is difficult We have used ultrasound to document the extent and number of plaques in 13 patients suffering from this disease. Sagittal and transverse scans of the penis were performed with a high-resolution (8 MHz), real-time ultrasound probe, with an integral water-bath Abnormalities were found in 12 patients, consisting of areas of increased reflectivity which were often multiple, with varied anatomical distribution. Thickening of the tunica albuginea was seen in 10 cases, lesions within the corpora cavernosa in nine cases, and lesions in the region of the intercorporeal septum in five cases. In four instances, there was acoustic shadowing distal to the lesion, and the presence of calcification was confirmed on the soft-tissue radiographs of all of these The method of ultrasound examination is demonstrated, the abnormalities illustrated, and the relevance of these findings to the treatment of the condition is discussed.

## ULTRASOUND-GUIDED BIOPSY TECHNIQUES

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Ultrasonically guided coarse-needle biopsies were carried out on 48 patients with suspected or previously demonstrated brain tumour Different techniques were tested. The best results were achieved using a special device for rapid movement of a 14 G cannula over an obturator with a 17 mm specimen sampling notch. The edges of the tip of the obturator as well as the corners of the sampling notch were rounded so that the needle could be introduced into the tissues without tearing it In 27 out of 30 patients it was possible to establish the diagnosis using the new technique Coarse-needle biopsies of other organs and lesions were carried out using a different technique A device for automatic movement of the two parts (the obturator and the cannula) was used With this technique it was, thus, possible to manoeuvre the transducer with one hand and with the other to perform the biopsy One hundred and seventy-five biopsies were taken from patients with carcinoid metastases or endocrine tumours and 27 biopsies of the spleen were taken with the aid of the device loaded with a 14 G needle Later, most biopsies were carried out using the instrument loaded with an 18 G needle· 175 biopsies on renal transplants, 24 on spleens, 22 on intra-abdominal or retroperitoneal lymph nodes and 74 on various liver tumours. The biopsy specimens were of very good quality and accurate diagnoses were achieved in 95% of cases. The complication rate was low when the 14 G needle was used; one patient underwent spelectomy because of bleeding and three required blood transfusion So far no complication whatsoever requiring surgery or blood transfusion has occurred after biopsy performed using the 18 G needle (The biopsy techniques are demonstrated on video )

## ULTRASOUND-GUIDED RENAL ALLOGRAFT BIOPSY WITH THE "BIOPTY" SYSTEM

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Renal allograft biopsy may be required to provide a histological diagnosis of graft dysfunction To minimise the risks of haemorrhage and graft damage, many centres, including our own, have hitherto adopted a policy of operative ("open") allograft biopsy We present our experience of a percutaneous renal allograft biopsy technique using a new automatic spring-loaded system (Radiplast Biopty) guided by real-time ultrasonography to localise the site of biopsy accurately The automatic mechanism moves the cannula and obturator of the Biopty-Cut needle a precise distance into the allograft in a projected line that is clearly displayed on the ultrasound image Thirty consecutive renal allograft biopsies were attempted in 27 cyclosporin-immunosuppressed recipients during episodes of renal dysfunction Ten biopsies were obtained with a 14 G (2 mm) needle, and 20 with an 18 G (1 2 mm) needle, producing tissue cores of lengths 20 mm and 17 mm respectively. Under direct ultrasound visualisation, the needle tip was positioned so that when the gun was fired, the inner notched obturator and outer cutting cannula were advanced in rapid succession over one another into the renal cortex, deliberately avoiding the medullary pyramids, pelvicalyceal system and hilar structures There were no complications apart from a single instance of transient haematuria. A complete core of tissue, adequate for histological diagnosis, was obtained at the first pass in 28 biopsies, and after a second pass in one other instance. There was one failure to obtain renal tissue, early in the series. We conclude that the Radiplast Biopty system used under ultrasound guidance offers a safe and reliable method for percutaneous renal allograft biopsy. A video-tape of the procedure is shown

## CLINICAL APPLICATIONS OF SONICALLY SENSITIVE NEEDLES IN FINE-NEEDLE ASPIRATIONS FOR CYTOLOGY

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Fine-needle aspiration has become an increasingly important method of reaching clinical diagnoses and allowing appropriate management decisions to be made Many factors affect the results but one of the most important is certainly that the material obtained comes from the lesion concerned Several methods of needle guidance have been developed, including biopsy guides for transducers, sonically sensitive needle tips, and roughened needle tips and shafts, etc. This paper concerns the clinical use of a sonically sensitive stilet which can be inserted into the aspiration needle The technical details of this have been described at previous BMUS meetings The needle system has been developed over the course of the last 3 years, during which we have performed 216 fine-needle aspirations on 180 patients and the system has been used in 57 of these patients Based on this experience the advantages of the needle in our practice have been determined (1) It allows accurate placing of the needle tip in the centre, or most suitable part, of a lesion. (2) It aids in directing the needle towards small or deep lesions by allowing the course of the needle to be more easily appreciated. (3) It allows the needle to be inserted at a site remote from the transducer, thus allowing a wider choice of needle insertion and scanning position. The benefits of using the needle and its value are discussed and illustrated with representative examples of relevant cases.

### ULTRASOUND IMAGING OF THE EYE THROUGH THE CLOSED LID USING A NON-DEDICATED SCANNER

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*Shrewsbury*

Eye scanning through the closed lid with general ultrasound equipment was initiated in a district general hospital to determine whether the technique is accurate in diagnosing ocular pathology. Two hundred consecutive scans were carried out on 184 patients. The examination was simple to perform and good images were produced. One hundred and thirty-eight abnormalities were demonstrated, 80 of which were not previously known, with one false positive. The latter was an incorrect interpretation of an abnormal scan, which was diagnosed as a tumour, but which proved to be haemorrhage. Ninety-four scans were negative, four of which were false negatives. Three of these were small, almost resolved vitreous haemorrhages and one was a small melanoma. The method proved to be sensitive (92%) and specific (99%) in the detection and exclusion of intra-ocular disease The investigation is, therefore, within the scope of the radiologist who does not have access to dedicated equipment

### APPLICATION OF ECHOGRAPHY TO THYROID SCREENING: RESULTS OF A PRELIMINARY STUDY

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The availability of echographic imaging systems operating at higher ultrasonic frequencies has made it relatively easy to obtain images of the thyroid gland which are of sufficient quality to raise the question of using them to screen the normal population for thyroid disease. Since April 1985 we have been conducting a preliminary study designed to assess the potential usefulness of echography in thyroid screening. The thyroids of 1248 people were examined, of which 612 presented with some problem of a superficial organ other than the thyroid (usually the breast) and 636 were completely asymptomatic The latter group were women attending a breast screening clinic. Thyroid examinations were performed as extensions of other ultrasound examinations already scheduled for the subjects. An Aloka real-time mechanical sector scanner, equipped with a 7.5 MHz water-delay scanning head, was used for all examinations, which were typically 20 s long. Final diagnoses of thyroid abnormalities were obtained with either aspiration cytology (sometimes ultrasound-guided) or open biopsy. Thyroid disease was detected in 202 of the subjects (16.2%), which included 10 cases (0.8%) of thyroid cancer. The mean age for the cancer cases was 49 years and the incidence of thyroid cancer was higher (1.3%) for subjects over age 40 years than for those under 40 years. Forty per cent of all cancers detected were non-palpable. The incidence of thyroid cancer found at autopsy in Japan is high: 14–28% compared (for example) with 6% in Sweden It is said that almost all such thyroid cancers remain occult. We did pick up, however, one non-palpable cancer (8 mm diameter) which had invaded the trachea. Since thyroid carcinoma can be cured by surgery we recommend that echography be used for mass screening of the thyroid.

### VALUE OF ULTRASOUND SCANNING IN THE PAROTID REGION

Allan T. Irvine, J. Browning-Smith, N. Stafford, P. R. Patel and G. Walsh-Waring

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Traditionally, sialography is the standard radiological method of investigating the parotid gland. In this study 37 patients with either palpable mass lesions in the parotid region or diffuse facial swelling were studied. In all cases of a palpable mass lesion the ultrasound examination could identify the mass, its site with reference to the gland and its internal characteristics. A variety of tumours were encountered, but there were no clear distinguishing ultrasonic features between benign and malignant tumours. Sialography was accurate in identification of a mass lesion in only 66% of cases. In patients with diffuse facial swelling the ultrasound was abnormal in those patients with gross sialectasis, but was normal in patients with only slight changes of sialectasis. Ultrasound would appear to have a useful role to play in the evaluation of a palpable mass lesion, but is limited in inflammatory disease of the parotid. The results are compared with the previous literature on the subject.

### THE ROLE OF ULTRASOUND IN THE ASSESSMENT OF UNILATERAL PAROTID SWELLING

J. V. Byrne and A. M. Whyte

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In assessing a parotid mass, radiological investigations aim to differentiate an intrinsic from an extrinsic lesion, a benign from a malignant tumour and to demonstrate the relationship of a tumour to the facial nerve. Conventional sialography is uncomfortable for patients and seldom alters their management. Computed tomography (CT) provides excellent anatomical delineation of the gland and surrounding tissues but sialographic contrast enhancement is required for isodense tumours and the identification of malignancy depends on there being evidence of local or metastatic spread. Ultrasonography using a 7.5 MHz or 5 MHz short-focus transducer was performed in 21 patients presenting with unilateral gland swelling. These investigations demonstrated intraglandular tumours in 15 patients, an extraglandular node mass in two patients and inflammatory disease in four patients Correct ultrasonic localisation of these lesions was confirmed by CT and/or surgical exploration. Histological diagnoses were obtained in 13 tumours, comprising 10 benign and three malignant lesions. Ultrasonography differentiated benign from malignant tumours in all but one instance. Failure to diagnose local invasion by this tumour was because of incomplete visualisation of its margin. Five of the 15 tumour patients, including the above, were further investigated by CT because malignancy was suspected or visualisation of the tumour margin was incomplete. The series included two patients with adenolymphomas, which both showed characteristic ultrasonographic signs The technique proved useful for inflammatory disease Abscesses were identified in two of three patients referred with swelling and signs of acute parotitis and a retention cyst in association with sialectasis in one patient. Ultrasonography provides a simple method of confirming the presence and position of an intraparotid tumour. The tumour's position relative to the facial nerve can be assessed. Characteristic sonographic features may be present and, provided tumour margins are completely visualised, benign and malignant tumour may be distinguished

# Veterinary ultrasound

**Chairman: W. R. Allen**
**Co-chairman: J. Cuthbert**

## Equine ultrasound

Investigation of equine ovarian cyclical changes by ultrasound scanning and rectal palpation, by J. R. Newcombe
Ultrasound imaging of soft-tissue structures in the equine limb, by J. S Boyd and C. Marr
Ultrasound in gynaecological abnormalities of the mare, by D. R. Ellis

### INVESTIGATION OF EQUINE OVARIAN CYCLICAL CHANGES BY ULTRASOUND SCANNING AND RECTAL PALPATION

John R. Newcombe

*Barracks Lane, Brownhills, West Midlands*

Before the introduction of ultrasound scanning to equine stud medicine, the investigation of changes occurring within the ovary and uterine lumen was largely limited to rectal palpation. The two most regular diagnoses made by the stud veterinarian are the detection of ovulation and early pregnancy. With the twin objectives of conserving the sexual energy of the stallion and of ensuring a high rate of conception in the mares with minimal time delay, it is essential that ovulation detection and early pregnancy diagnosis are highly accurate Experienced practitioners can achieve this high standard but there remain some problem areas. The accurate detection of twin ovulations from the same ovary and the early recognition of bilateral twin pregnancies is often difficult. Unilateral twin pregnancy cannot be detected at any stage by rectal palpation and there are always a few awkward mares in which pregnancy diagnosis may not be possible until at least 30 days. Ovulation detection per rectum depends on the palpation of one or more follicles in the ovaries and their re-examination after a suitable interval In this time one or more follicles may have disappeared to be replaced by a soft spongy or rubbery area Not infrequently the corpus luteum (corpus haemorrhagicum (CH)) is palpable as a smooth, non-spherical body, smaller than the follicle and more solid and rubbery in texture In other cases there is nothing palpable within the ovary and, particularly when ovulation has occurred from a relatively small follicle, the practitioner may assume that the follicle has regressed and "disappeared" within the ovarian stroma Unfortunately it is not unusual for the corpus luteum (CH) to form identically in shape, size and texture to the original follicle Very occasionally follicular rupture does not occur, the follicle continues to grow probably because of intrafollicular haemorrhage, luteinisation follows and the so-formed "luteinised follicle" appears to function as a corpus luteum Not infrequently two or more significant follicles are palpable in the same ovary. Even by very regular monitoring it is often difficult to decide whether one or both, or, indeed, if either follicle has ovulated.

The ultrasound scanner has made it possible to visualise, measure and count all follicles down to about 5 mm in diameter Two large follicles in close apposition may appear as one by rectal palpation but are clearly "twin" follicles on the screen. Follicular haemorrhage gives a "snow storm" appearance. The very recent ovulation may be difficult to visualise but the early CH appears as a very dense amorphous area. As the CH organises, lacunae may appear and sometimes the solid luteal border may be clearly outlined against a large lacuna Multiple ovulations are diagnosed by the disappearance of two or more follicles, but twin corpora lutea in close apposition may appear as one The paper illustrates various other interesting variations taken by polaroid photography

### ULTRASOUND IMAGING OF SOFT-TISSUE STRUCTURES IN THE EQUINE LIMB

John S. Boyd and Celia Marr

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Using B-mode two-dimensional real-time ultrasound scanning with a 7 5 MHz linear transducer, the soft-tissue structures of the equine limb were examined to build up an impression of the normal anatomy of the region The relationship and configuration of the tendinous structures and their synovial coverings were imaged ultrasonically in both live animals and limbs taken from fresh cadavers. Markers were placed in the tendons of the cadavers and, after freezing and sectioning, photographs of these structures were produced to correspond to the ultrasound images. By this method a better understanding of the regional anatomy could be ascertained A series of horses with traumatic lesions of the tendinous structures of the lower limb was examined with a 7 5 MHz linear transducer and the results recorded Where possible these animals were followed for varying periods of time to assess changes occurring in the affected region in response to treatment and rest A number of animals were examined at post-mortem examination, where a correlation between necropsy findings and ultrasound images could be made.

### ULTRASOUND IN GYNAECOLOGICAL ABNORMALITIES OF THE MARE (SOME OBSERVATIONS ON ENDOMETRIAL CYSTS IN MARES)

D. R. Ellis

*Newmarket*

Endometrial cysts have been recognised in older mares for many years, but the recent introduction of ultrasound echography into routine stud-farm gynaecology has shown that they have a higher incidence than was suspected They are certainly age-related but their effect on fertility, measured as live foal production, is questionable. From the scanning records of 2670 mares during the 1983, 1984 and 1985 stud seasons, 233 (8 72%) had endometrial cysts diagnosed echographically. Their average age was 14.3 years and 73% were foaling mares The types and sites of cysts are described and 43.5% of cysts were single and closely associated with the fetal sac during the first 35 days of pregnancy Multiple cysts occurred in 0 86% of the mares scanned. Persistence of cysts was less than expected, as 64% of 22 mares with cysts which were barren at first scanning showed the same pattern and type of cysts when scanned again following further covering Similarly, only 59 5% of 42 mares which had cysts in two or three of the years in this study had a consistent pattern of cysts. Live foal production of the mares with endometrial cysts in 1983 and 1984 was 17 8% less than the mares scanned but without cysts. The latter group had a lower average age (9 years) than the 14.3 years of those with cysts whose live foal production of 65.7% was slightly better than the 62% (var 60–70) recorded for 14- and 15-year-old mares by Jeffcott et al (1982) in their 1973–79 survey There was a higher number of early fetal losses or absorptions (8.6%) among the mares with cysts Differentiation of cysts from twin pregnancies is discussed

## Ultrasound in exotic animals

Pregnancy and disease diagnosis in exotic animals, by G H. du Boulay and C. L. Wilson

### PREGNANCY AND DISEASE DIAGNOSIS IN EXOTIC ANIMALS

G. H. du Boulay and C. L. Wilson

*London Zoo*

Ultrasound was first introduced at London Zoo as a potential aid to breeding programmes in 1983, but its use in disease diagnosis very soon became apparent. It has naturally been difficult to gain experience of normal anatomy because the circumstances are against routine screening, and the numbers of individuals examined in any species is very small Not surprisingly, much of our experience of disease is in the ovaries and uterus, but because animals find difficulty in explaining the site of their illness, many of the examinations involve as wide a search as is practicable. The limiting factors being, co-operation, potential dangers of sedation and fur! Anecdotal experiences described are drawn from the following, arranged here by topic.

| | |
|---|---|
| Land mammals | |
| Lion-tailed macaque: | endometriosis, pyometrium, ovarian tumour. |
| Gemsbok. | ovarian cyst |
| Giant panda: | ascites, ileus |
| Lowland gorilla: | putative large-bowel obstruction, unsuspected pregnancy |
| Orangutan and chimpanzee: | pregnancy management in spite of maternal antics. |
| Common marmoset: | fetal hydrocephalus and death |
| Marine mammals | |
| Dolphin: | early and late pregnancy, normal liver. |
| Killer whale: | fatty replacement of normal liver tissue |
| Reptiles | |
| Especially snakes: | abscess, aortic aneurysm, obstruction in oviduct, fertility of eggs |

## Ultrasound in farm and domestic animals

**Chairman: D. G. G. Jackson**
**Co-chairman: H. B. Meire**

The use of ultrasound in commercial sheep and cattle enterprises, by A. J. F. Russell
The use of ultrasound in a mixed/small-animal practice, by P. M. Parry-Smith
The use of real-time ultrasonography in pig herds, by G. H. Jackson
The uses of a sector scanner in mixed practice, by D McKeown
The use of ultrasound in evaluation of diseases of the liver and kidneys in the dog and cat, by F. Barr, C. Gibbs and P. Wotton
Ultrasound imaging of abdominal structures in domestic animals, by C. Marr and J. S. Boyd
Echocardiography in dogs and cats by P. R. Wotton, F. J. Barr and C. Gibbs
False tendons in the canine left ventricle. two-dimensional echocardiographic/anatomic correlation, by J. M. Beattie and C. G. Blomqvist

### THE USE OF ULTRASOUND IN COMMERCIAL SHEEP AND CATTLE ENTERPRISES

A. J. F Russell

*Hill Farming Research Organisation, Penicuik, Midlothian*

Trials conducted in early 1983 showed that real-time ultrasonic scanning could be used to diagnose pregnancy and determine fetal numbers in sheep safely, accurately and rapidly. The use of the technique has been readily accepted by the sheep industry and it is estimated that in the 1985–86 winter some 2 000 000 ewes were scanned in the United Kingdom by about 70 commercial scanning operators. Gestation length in the sheep is 147 days and accurate determination of fetal numbers can be made from approximately 50 days to 100 days. Levels of proficiency vary between operators, but many of the more experienced operators consistently achieve accuracies of 98% or better. Rate of scanning varies from 60–80 per h, where fetal numbers in excess of two have to be determined, to about 120 per h where ewes require to be classified only as single- or multiple-bearing. Skilled operators can scan more than 40 000 ewes in 10–12 weeks. Most operators use linear-array instruments but there has recently been a marked move to sector scanners, which enable ewes to be scanned in the standing position, thus reducing labour requirements; problems of poor image quality resulting from intestinal gas are also lessened The main benefits of ewe scanning to the sheep farmer are: savings in feeding costs, arising principally from the identification of non-pregnant ewes; reduced lamb mortality as a consequence of improved birth weights; reduced ewe mortality as a result of fewer metabolic disorders, and simplified management at lambing. More recently, real-time ultrasonic scanning has been used with an intrarectal probe to diagnose pregnancy and estimate fetal age in cattle. Gestation length in the cow is 280–285 days, pregnancy can be diagnosed accurately from 30 days or less and fetal age estimated between 30 days and 140 days. On a herd basis, about 60% of cows calve within 3 days of the predicted date and 90% within 10 days.

## THE USE OF ULTRASOUND IN A MIXED/SMALL-ANIMAL PRACTICE

P. M. Parry-Smith

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A BCF sector scanner has been in regular use in this practice since April 1986, a few practical points and early results are briefly discussed Pregnancy diagnosis in the dog, particularly relating to poor reproductive performance, has been invaluable, and a high degree of accuracy has been achieved The problem of the time of scanning related to gestational stage is discussed The use in cats has been limited Other uses in dogs have been the diagnosis of uterine disorders, abdominal tumours and conditions of the bladder. Hopes for the future include location of foreign bodies and further investigations of tumours. The use in horses has been very valuable and direct comparison with linear scanners had led to the conclusion that this machine's advanced features make it very worthwhile considering acquiring one in a busy mixed practice, especially as it is extremely suitable for the examination of sheep and goats.

## THE USE OF REAL-TIME ULTRASONOGRAPHY IN PIG HERDS

G. H. Jackson

*Meat and Livestock Commission, Bletchley*

The ideal method of pregnancy diagnosis for sows would be cheap and simple to use. It would give a result at the time the test was carried out and within 18 days of service. Because conception rates in pig herds are usually above 80% the method would have to be highly accurate in detecting pregnancy. During 1985 and 1986 real-time ultrasonography was evaluated for diagnosing pregnancy in a large pig herd. An initial study showed the technique should be highly accurate 24 days after service Frequent visits were made to the herd when sows were tested 24–38 days after service Sows were tested in the standing position using a sequential linear-array scanner equipped with 3.5 MHz transducer The transducer was placed on the right abdominal wall when testing the sow To date, farrowing results from a total of 452 tested sows are available Of 419 diagnosed pregnant, 412 farrowed or aborted while seven (1.7%) failed to farrow Of 33 diagnosed not pregnant none farrowed to the due service date. During the course of this work, sows with a number of other conditions were examined by real-time ultrasonography. These included sows subsequently found to have cystic follicles, mummified fetuses and endometritis The author considers that real-time ultrasonography can be a useful technique to diagnose these conditions in sows. It is common practice for pig producers to use the A-mode or Doppler ultrasound principle to diagnose pregnancy in sows. The author is currently comparing a real-time ultrasound machine with an A-mode ultrasound machine to see what advantage one has over the other for the pig producer

## THE USES OF A SECTOR SCANNER IN MIXED PRACTICE

D. McKeown

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David McKeown is a partner in a mixed practice in North Antrim. The sector scanner was purchased to cater for the large number of breeding ewes within the practice. During the months of November and March, 16 000 ewes were scanned with an accuracy of about 95% in differentiation of barren, single- and twin-bearing ewes Since March the scanner has been used in pregnancy diagnosis in pigs, cattle, mares and dogs allowing pregnancy to be detected between 20 and 30 days Rams' testicles and dogs' livers are among the other organs examined. Slides are shown of the pictures produced

## THE USE OF ULTRASOUND IN EVALUATION OF DISEASES OF THE LIVER AND KIDNEYS IN THE DOG AND CAT

F. Barr, C. Gibbs and P. Wotton

*University of Bristol Veterinary School*

Diseases of the liver and kidneys are relatively common in small animals. However, conventional radiography is of limited use in evaluating these organs, showing changes only in size and contour or gross changes in density. Contrast techniques such as intravenous urography, cholecystography and angiography may give additional information Diagnostic ultrasound may potentially complement conventional radiography by giving information on the internal architecture of parenchymatous organs. The normal ultrasonographic anatomy of the liver in the dog and cat is broadly described. Focal hepatic neoplasms, either single or multiple, are readily seen. The most common ultrasonographic picture seen in cases at Bristol University Veterinary School has been that of multiple, irregular echolucent patches scattered throughout the substance of the liver. Biliary disease is less common than in man, with gallstones a rare occurrence, but the ultrasonographic appearance of the biliary tree in cases of obstructive jaundice is characteristic, with multiple irregularly branching vessels with echogenic walls visible within the liver A distended gallbladder should also be seen Hepatic venous congestion is a relatively common finding, and the prominent pattern of distended hepatic veins is readily seen. Diffuse hepatic disease, such as diffuse neoplasia, fibrosis, hepatitis and fatty change are less easily characterised. Examples of cases are shown.

The normal ultrasonographic anatomy of the kidney in the dog and cat is also described Chronic infection with associated dilatation of renal pelvis and ureter and distortion of the normal renal architecture can be appreciated, as can obstructive lesions resulting in hydronephrosis and hydroureter. Renal neoplasms can also readily be seen: an important fact as these may be clinically silent Diffuse renal disease has again proved difficult to characterise. Examples are shown. Ultrasound-guided biopsy is a logical step in definitive evaluation of lesions in these organs, and the potential uses of this technique are discussed.

## ULTRASOUND IMAGING OF ABDOMINAL STRUCTURES IN DOMESTIC ANIMALS

Celia Marr and John S. Boyd

*University of Glasgow Veterinary School*

Using B-mode two-dimensional real-time ultrasound scanning with both linear and sector probes, the abdomens of various domestic animals were examined to exhibit both normal topography and organ structure. To assist in interpretation, fresh cadavers were deep-frozen and then sectioned in planes that corresponded with the ultrasonic images. By this method the operators were initially trained to identify the structures seen on the ultrasound pictures. The variation in organ textures when imaged ultrasonically was recorded and also significant topographical landmarks highlighted. Using this information a series of clinical cases was examined with both linear and sector probes of 3 MHz, 5 MHz and 7.5 MHz and pathological changes occurring in organs such as liver, spleen and prostate were demonstrated Where the animals arrived at a post-mortem examination, the interpretation of the ultrasound image could be evaluated by comparison with the necropsy findings Pregnancy diagnosis was also carried out percutaneously in a number of animals of differing species and a record made of the times that pregnancy could be identified and also changes in fetal growth patterns were monitored.

## ECHOCARDIOGRAPHY IN DOGS AND CATS

P. R. Wotton, F. J. Barr and C. Gibbs

*Departments of Veterinary Medicine and Surgery, University of Bristol*

This paper reviews the contribution made by the use of B-mode real-time, cross-sectional ultrasound examination in the investigation and management of referred cases of cardiac disease in dogs and cats presented to the University of Bristol's Departments of Veterinary Medicine and Surgery over a 7-month period. The methods of examination, problems encountered and the equipment used for these examinations are discussed. During this time 175 ultrasound investigations have been carried out, of which 85 were cardiac, including 69 dogs, 12 cats, three horses and one goat Echocardiography has been found to be particularly helpful in cases of cardiomyopathy in dogs and cats, pericardial disease in dogs, certain types of congenital cardiac malformation (particularly aortic stenosis and ventricular septal defect) and one suspected case of endocarditis Examples of some of these cases are presented It is hoped that further experience with this technique, increasing familiarity with echocardiographic anatomy, the use of electrocardiographic triggering and the development, by ourselves and other workers, of a broad range of normal values for echocardiographic parameters in the various species, will make the technique even more valuable. In particular, the more accurate quantification of myocardial contractile function will be especially helpful in assessing cases of myocardial disease and in following the progress of therapy.

## FALSE TENDONS IN THE CANINE LEFT VENTRICLE: TWO-DIMENSIONAL ECHOCARDIOGRAPHIC/ANATOMIC CORRELATION

J. M. Beattie and C. G. Blomqvist

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Left ventricular false tendons are composed of Purkinje fibres and represent intracavitary ramification of the peripheral cardiac conduction system. Although a normal feature of ungulate and canine hearts, their presence in the feline heart has been linked with cardiomyopathy. In primates the prevalence and morphology of these structures remain ill-defined, but in man they have been variously associated with the generation of systolic murmurs, ventricular arrhythmias and atypical chest pain. To assess the clinical potential of ultrasound in identifying false tendons, we examined their morphology in 10 adult mongrel dogs by two-dimensional echocardiography and at subsequent necropsy. Using a 90° phased-array sector scanner, echocardiograms were recorded from standard parasternal and apical imaging planes. To facilitate classification, left ventricular regions were defined as apical, mid-ventricular and basal by criteria of the American Society of Echocardiography. False tendons arising and inserting within the same ventricular region were classified as transverse and between adjacent ventricular regions as diagonal. Use of the same morphologic classification at post-mortem examination facilitated echocardiographic/anatomic correlation. At necropsy, false tendons were identified in all 10 canine hearts and were of relatively uniform morphology. Nine dogs exhibited two false tendons This was a combination of mid-ventricular/basal diagonal and mid-ventricular transverse in five, duplicated mid-ventricular transverse in three and duplicated mid-ventricular/basal diagonal in one. In the remaining dog, an isolated mid-ventricular transverse tendon was evident. These morphological variants were confirmed by echocardiography in nine dogs and were well defined in six, most detail being evident in short-axis images. This suggests that this technique may be useful for further study of such structures in the human clinical population

# Posters

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## ULTRASONIC EQUIPMENT EVALUATION PROJECT

P. D. Clark

*Department of Clinical Physics and Bio-engineering, Glasgow*

The poster describes the Ultrasonic Equipment Evaluation Project, which commenced in June 1986 The project is based at the Department of Clinical Physics and Bio-engineering of the Greater Glasgow Health Board, taking advantage of many years of ultrasound experience in the city where the contact medical ultrasound scanner was born. The project is funded by the Common Services Agency of the Scottish Health Service. At present, new models of ultrasound scanners are evaluated on site at the hospital where they were purchased. As the project develops there may be a move towards borrowing new equipment from manufacturers for evaluation at a central laboratory.

Four aspects of the project are described and illustrated in the display The first is background and organisation of the project.

The second is evaluation, the features of ultrasound equipment to evaluate are·
(a) capital cost,
(b) maintenance costs and arrangements,
(c) reliability,
(d) compliance with safety standards,
(e) imaging performance,
(f) installation experience,
(g) operational experience, and
(h) clinical experience

Features (a) to (e) are expressible quantitatively In order to be a truly objective measure the figures for each feature should be seen in relation to the distribution of figures for that feature over the range of scanners available. Such information on the normal ranges of figures is available from various sources for features (a) to (d), but feature (e), the imaging performance of the scanner, is a set of figures which the project itself generates for each scanner As the project progresses, the extent to which imaging performance can be made a meaningful objective measure will improve. This means, for example, that the imaging performance feature of the first report produced by the project will be more easily understood when, say, 10 reports have been produced with which to compare it. It is of course important that a standardisation of measurement procedures is maintained throughout the reports. For this purpose the Cardiff Test System has been used. Features (f), (g) and (h) are a combination of subjective and objective comments and are presented impartially for the reader to make his own value judgement.

The third aspect is the equipment (and measurement procedures?), with description of the Cardiff Test System and the Beca System, and a Doppler phantom? The fourth aspect is that of the results/list of available reports. a collation of the results of imaging performance

## A PVDF NEEDLE HYDROPHONE FOR *IN-VIVO* TISSUE MEASUREMENTS

J. D. Aindow, P. A. Robbins and D. Deogan

*Departments of Medical Physics, Dorset County Hospital, Dorchester, Dorset and Electronics Department, Polytechnic of Wales, Pontypridd*

Despite the rapid advances in ultrasound scanner technology during the last decade, the scientific literature still contains very few data on the acoustic properties of human tissue that have been measured by *in-vivo* techniques. Accurate *in-vivo* ultrasonic data for most tissues are virtually non-existent In order to determine some of these parameters we have developed a needle hydrophone which may be used for *in-vivo* measurements of attenuation and velocity The device has been designed specifically to provide data acquisition during routine interventional ultrasound procedures and so provide a source of data that is both statistically reliable and accurate. The construction of the hydrophone and associated electronics are outlined, together with results of calibration procedures. Encouraging preliminary measurements of the *in-vitro* performance of the device are presented

### "HORIZONTAL" CALIPER ERRORS IN SECTOR SCANNERS

J. M. Pelmore and A. C. Graebe

*Medical Physics Department, Leicester Royal Infirmary*

In recent years ultrasonic sector scanners have been increasingly used for making accurate serial measurements in obstetrics, abdominal imaging and cardiology. Experience has shown that "horizontal" as opposed to "vertical" caliper measurements on this type of instrument are not quite as reliable as those taken with linear arrays. Three types of instrument were considered. mechanical sector scanners, phased array scanners, and curved linear-array scanners. A survey was made of examples of these three types of scanners in Leicestershire District. Five different test objects were evaluated for making the required measurements wire phantom in open-top tank; wire phantom in tank with membrane window, tissue-mimicking test object with membrane window; AIUM test object with 1.5 mm perspex window; and Cardiff test object with 1.0 mm polyethylene window.

The most generally reliable method for checking caliper measurements on these types of scanner is a wire phantom mounted in an open-top tank. A test object with a thin membrane acoustic window may prove satisfactory if carefully used. Caution is necessary with test objects fitted with a thick window because correction may need to be made for refraction effects Some possible sources of error that can occur with all five test objects are illustrated. Detailed results are tabulated of the "horizontal" caliper errors found on the three different types of sector scanner.

### A STUDY OF ULTRASONIC DEPTH PENETRATION

J. M. Pelmore and A. C. Perkins

*Medical Physics, Leicester Royal Infirmary and Medical Physics, Queens Medical Centre, Nottingham*

The ultrasonic depth penetration has been measured on a variety of ultrasonic imaging systems in Leicester and Nottingham hospitals using three different test objects. The imaging systems tested include linear arrays, phased arrays, curved linear arrays, mechanical sector scanners and manually operated static scanners. The types of test object used were a perspex block, a tissue-mimicking test object and a polyethylene step-wedge The relative practical merits of the three different test objects are discussed and comments are made about the relative performance of different imaging systems.

### AN A-TYPE ULTRASONIC MICROPROBE FOR USE IN STEREOTACTIC NEUROSURGERY

D. A. Causer

*Midland Centre for Neurosurgery*

An ultrasonic microprobe has been developed at the Midland Centre for Neurosurgery and Neurology for use in conjunction with stereotactic apparatus designed for brain surgery. An A-type probe, 30 cm long and 3 mm in diameter, has been constructed and tested within the Department of Medical Physics The crystal operates at 10 MHz and the results of *in-vitro* measurements of the probe performance are shown. The body of the probe is constructed from 11-gauge stainless-steel needle tubing, to which the front face of the crystal is connected, and the tubing is earthed The crystal is 2 mm in diameter and its back face is connected to an electrode which passes down the body of the instrument insulated from it by rubber sleeving. The crystal is mounted on a tungsten-Araldite backing which has been moulded for the purpose in the physics laboratory. The whole of the tungsten-Araldite/crystal assembly is covered with a layer of Araldite for insulation purposes. The probe is isolated from the electronics for safety purposes by the use of an isolating pulse transformer

### VALUE OF CONTINUOUS-WAVE DOPPLER IN THE ESTIMATION OF PULMONARY ARTERY PRESSURE IN CHILDREN WITH SYSTEMIC TO PULMONARY ARTERY SHUNTS

S. A. Qureshi, Joanna H. Dangel, Roberta M Bini, R. Arnold and J. L. Wilkinson

*Royal Liverpool Children's Hospital, Liverpool*

Twelve children aged between 8 months and 12 years (mean 55 months) underwent measurement of the pulmonary artery (PA) pressure by continuous-wave Doppler (CWD) echocardiography, cardiac catheterisation or at operation The systolic PA pressure was estimated by subtracting the pressure drop obtained across the shunts by CWD from the systolic brachial artery pressure measured by cuff sphygmomanometer. Four of the children had persistent arterial ducts, three had undergone previous Waterston shunts for pulmonary atresia with intact ventricular septum and five had Blalock-Taussig shunts for tricuspid atresia (two), Fallot's tetralogy (one), pulmonary atresia with atrioventricular septal defect (one) and transposition of the great arteries, ventricular septal defect and pulmonary stenosis (one). The systolic pressure drop between the brachial artery and PA by CWD ranged from 49 to 119 mmHg (mean $\pm SD = 73 \pm 20$) compared with 54 to 108 mmHg ($75 \pm 17$) at catheterisation or operation ($p$ = NS) The correlation coefficient, $r$, was 0.91. The systolic PA pressure by CWD varied between 20 and 40 mmHg ($30 \pm 7$) compared with between 8 and 37 mmHg ($24 \pm 10$) at catheterisation/operation ($p$ = NS) and $r$ was 0.64. The PA to systemic artery systolic pressure ratio by CWD was between 0.15 and 0.4 ($0.3 \pm 0.08$) and that at catheterisation/operation was between 0.10 and 0.36 ($0.24 \pm 0.09$) ($p$ = NS). The $r$ value was 0.49 It is concluded that CWD provides a useful non-invasive method of estimating the systolic PA pressure from the pressure drop obtained across the systemic to PA shunts

### USEFULNESS AND RELIABILITY OF DOPPLER ULTRASOUND IN THE NON-INVASIVE DETERMINATION OF VALVE GRADIENTS AND PULMONARY ARTERY PRESSURE

M. G. Cheesman, R. John, J. Thomas and V. J. Redding

*Regional Cardiac Centre, Groby Road Hospital, Leicester*

Continuous-wave and pulsed Doppler ultrasound have been used as adjuncts to two-dimensional echocardiography in patients presenting for cardiac catheterisation at this centre over the last 6 months. Doppler studies were undertaken under "outpatient" conditions either the day before invasive study or during a previous clinic attendance. Mitral valve gradients obtained by Doppler ultrasound correlated well with those found at catheterisation ($r = 0.95$, $n = 11$) and in another seven patients the finding of no significant gradient was confirmed, despite markedly abnormal valves on echocardiography Six of these 18 patients had multivalvular disease. Aortic valve gradients obtained by Doppler ultrasound correlated less well ($r = 0.78$, $n = 11$) than did the mitral valve gradients, and in two cases there were clinically important differences in the results obtained by the two methods In 10 additional patients the Doppler ultrasound finding of no significant gradient was confirmed at invasive study, despite abnormal echocardiographic images. In a further four patients the aortic valve could not be crossed at catheterisation, although Doppler studies indicated a gradient of at least 65 mmHg in each case; three of these patients have now been submitted to surgery, and severe calcific aortic stenosis was found in each case. Pulmonary artery pressure was estimated from the velocity of tricuspid regurgitation in a wide diversity of cardiac disease; correlation with values obtained at right-heart catheterisation were good ($r = 0.95$, $n = 14$). Doppler ultrasound is a powerful non-invasive aid to the diagnosis of a wide range of cardiac disease under normal practice conditions

## THE CLINICAL VALUE OF DOPPLER ULTRASOUND STUDIES OF THE HEPATIC VEINS

H. B. Meire and S. Coates

*King's College Hospital, London*

The blood flow patterns in the hepatic veins are influenced by several factors, including liver blood supply, liver disease and the pulse waves conducted from the right atrium into the inferior vena cava. Knowledge of the normal patterns can enable the ultrasonologist to suggest a number of specific diagnoses when abnormal patterns are observed The display includes graphic displays of the normal hepatic-vein signals and examples of the wide range of alterations in these caused by a number of cardiac and hepatic disorders.

## HEPATIC CYSTS WITH INTERNAL SEPTATIONS: AN ULTRASONIC DIFFERENTIAL DIAGNOSIS

A. N. Khan and R. A. L Bisset

The ultrasound scans of 45 patients with apparent cystic hepatic mass lesions with internal septations were reviewed Ultrasonography was accurate in demonstrating cyst morphology, but appearances were non-specific and a diagnosis could be made from the ultrasonic appearances alone in only one of the 45 cases (a hydatid cyst with the characteristic cyst within a cyst appearance). Correct diagnoses were offered in all but two cases (95.5%) when the results of sonography were considered in conjunction with the clinical history, examination and haematological investigations. No new ultrasonic characteristics were described and signs which were previously thought to narrow the differential diagnosis, for example fluid-fluid levels within the cysts, were seen in both benign and malignant lesions Pathological diagnoses were known in all 45 cases. There were 15 cases of metastases. pancreas (four), colon (four), ovary (two), stomach (two), bronchus (two) and leiomyosarcoma (one) There were 11 cases of infective lesion· hydatid cysts (seven) and pyogenic abscess (four). There were six cases of benign congenital cysts. There were 13 cases where lesions contiguous with the liver could not be differentiated from intrahepatic lesions: subphrenic abscess (three), ligamentum teres abscess (one), empyema and phlegmon of gallbladder (three), pancreatic pseudocyst (three), subhepatic haematoma (two) and benign ganglionic tumour of the adrenal (one)

The paper concludes that ultrasonography is an accurate method of demonstrating hepatic cysts with internal septations but appearances are often non-specific and there are at least 39 causes of complex hepatic cysts in the world literature. In everyday clinical practice, metastatic malignancy, infection and congenital cysts account for the majority of lesions seen

## THE AETIOLOGY OF ACUTE PANCREATITIS

P. Hammond

*Walsgrave Hospital, Coventry*

This poster depicts the varying aetiology of a number of cases of acute pancreatitis encountered in one ultrasonic department. The images are cartoon sketches of patients experiencing· gallstone pathology, alcoholic sequelae, drug therapy, pancreatic traumatic compression, endoscopic retrograde cholangiopancreatography, translumbar aortography and viral infection

## MEASUREMENT OF TIBIAL TORSION BY ULTRASOUND: A NEW TECHNIQUE

R. A. Carver, B. Joseph, R. K. Levick M. J. Bell and W. J. W. Sharrard

*Department of Radiology and Department of Orthopaedics, Children's Hospital, Sheffield*

Tibial torsion is encountered in a number of childhood conditions, particularly where there is neurological impairment, such as spina bifida and cerebral palsy. Such torsion impedes efforts at locomotion and therefore correction is advantageous A number of methods of measurement of tibial torsion have been devised, both clinical and radiological, none is very satisfactory. Computed tomography (CT) is the most accurate but entails a significant radiation dose. In this paper, a method of measuring tibial torsion by ultrasound is presented which is shown to be no less accurate than CT The difficulties encountered and sources of error are also described.

## RECENT DEVELOPMENTS IN THE ULTRASONIC ASSESSMENT OF PERI-OVULATORY CHANGES AND THE INCREASING ROLE OF ULTRASOUND IN THE MANAGEMENT OF FEMALE INFERTILITY

B. Smith, I. Craft, C. Keegan, J. Evans and E. Fincham

*Department of In Vitro Fertilisation and Fertility Studies, Humana Hospital Wellington, London*

Historically, the role of ultrasound in the management of female infertility has been restricted to the measurement of follicle number and size and the identification of collapse of the follicle signifying ovulation. Ultrasound assessment of approximately 8000 natural and stimulated ovulatory cycles has resulted in a more detailed appreciation of ovarian and endometrial changes surrounding ovulation and implantation. The ultrasonic parameters used to monitor an ovulatory response at present include follicle size and range of sizes, follicular growth gradients, endometrial thickness and textural appearances, rate of endometrial development and endocervical changes, as well as detailed studies of follicle wall/content changes. Improvements in transducer design, signal processing and scanning techniques have resulted in visualisation of follicular content and wall characteristics The growth rate of follicles, in both natural and stimulated cycles, is linear only during the early proliferative phase, with a tendency towards a continually increasing rate of development within the peri-ovulatory period The pre-ovulatory follicle is uniform in outline, becoming irregular with crenations of its wall, often showing evidence of oedematous changes immediately before ovulation. Cellular debris becomes more evident and often the culumulus oopherous mass is identified shortly before ovulation takes place. Advances in grey-scale capability enable visualisation of endometrial changes in addition to ovulatory changes within the ovary itself The endometrium is assessed not only in terms of quantitative changes in its thickness but also qualitative variations in grey-scale appearances. The latter is achieved by comparing the reflectivity of the endometrium with that of the surrounding myometrium. Distinct patterns are recognised in observing cyclical changes of the endometrium resulting in better judgment regarding the quality of an ovulatory response. In clinical terms this has greatly improved the timing of HCG administration before *in-vitro* fertilisation/"tubesperm-egg-transfer" or artificial insemination techniques.

## THE VALUE OF VAGINAL ULTRASOUND IN MONITORING *IN-VITRO* FERTILISATION PATIENTS

R. K. Goswamy, G. Williams and P. C. Steptoe

*Bourn Hall Clinic, Bourn Hall, Bourn, Cambridge*

This paper presents data on patients monitored for *in-vitro* fertilisation treatment in cycles stimulated by clomiphene/human menopausal gonadotrophins (HMG) and/or Metrodin (FSH) (Serono) therapy. The patients included in this study are those where follicular visualisation was inadequate or considered extremely difficult using traditional abdominal sector ultrasonography. Our data indicate that image quality, accuracy of follicular measurement, and adequate visualisation of follicles is possible only with vaginal ultrasonography in most cases. A detailed analysis of the reasons for poor abdominal imaging (*i.e.* abdominal scarring, severe adhesions in the pelvis and poor bladder control) compared with results achieved with vaginal monitoring are presented.

## LOCATION OF IMPLANTATION SITE IN PREGNANCIES RESULTING FROM *IN-VITRO* FERTILISATION

G. Williams, R. K. Goswamy and P C. Steptoe

*Bourn Hall Clinic, Bourn Hall, Bourn, Cambridge*

This paper presents data on patients who were scanned on Day 35 (post-oocyte recovery) following *in-vitro* fertilisation (IVF) therapy. All patients had been stimulated by clomiphene and human menopausal gonadotrophins for their treatment cycle and therefore multiple pregnancies are included in this survey Preliminary data on 88 patients and involving 126 gestation sacs indicate that most IVF pregnancies result in high or middle implantations. We have had low implantation in only two cases. A detailed analysis of the possible reasons for high implantation in IVF and correlations between implantation sites and pregnancy outcome are presented.

## TRANSVAGINAL ULTRASOUND-DIRECTED OOCYTE RECOVERY IN AN *IN-VITRO* FERTILISATION PROGRAMME

R. K. Goswamy, P. C. Steptoe and D. B. Cowan

*Bourn Hall Clinic, Bourn Hall, Bourn, Cambridge*

Several papers have described ultrasound-directed oocyte recovery routes using abdominal ultrasound probes. We are evaluating a vaginal probe with a view to using this for all patients requiring ultrasound-directed oocyte recovery All patients included in this study were noted to have laparoscopically inaccessible ovaries, partially accessible ovaries, or gave a history of difficult laparoscopies in the past With experience of more than 100 such procedures, we wish to present the results of patients undergoing this procedure from July 1, 1986, onwards. Preliminary data indicate an extremely high oocyte recovery rate (6.5 oocytes per patient) and an extremely efficient recovery rate per follicle aspirated (0.96). In comparison with previously reported ultrasound-directed methods we consider this procedure far superior. We are convinced that vaginal ultrasound-directed oocyte recovery will replace all other forms of ultrasound-directed oocyte recovery Whether this will replace laparoscopic oocyte recovery requires further evaluation.

## THE EFFECT OF "ROUTINE" ANTENATAL ULTRASOUND ON THE DIAGNOSIS OF CONGENITAL HYDRONEPHROSIS

J. C. Shanahan, H. Huang and J. A. Egginton

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Over a 3-year period, 22 fetal renal abnormalities were identified in 16 531 pregnancies, 21 being hydronephroses. While the number of patients scanned increased in consecutive years from 69%, through 85%, to near 100%, the number of renal lesions has risen sharply from four, through six, to 12, and is attributable to increasing skill on the part of the scanning radiographers rather than advances in equipment Post-natal investigation distinguished the two cases of extrarenal pelves and two of reflux not requiring surgery of 19 of the original cases available for study. The records of all renal tract investigations in children of corresponding age presenting over the same 3 years revealed 15 further children with similar urinary tract problems, including one presenting at birth with urine ascites. Eight of them had had reportedly normal antenatal scans. While the number of possible missed diagnoses showed no improvement from year to year, being two, one and five respectively, the number of true false negatives cannot be determined. Timing of scans can be important as well as variable tract distension both antenatally and post-natally Of the eight who re-presented, six required surgery and were, therefore, not insignificant. Recent *in-utero* identification of lesser degrees, as well as greater numbers of hydronephroses, has resulted in more cases of posterior urethral valves, megaureter and reflux being identified relative to the previously more common PUJ obstruction. In the study population antenatal identification has resulted in only four such children presenting in the neonatal period Overall figures also reflect a rise in the number of renal problems being identified in childhood, independent of antenatal scan

## ULTRASOUND IMAGING OF REPRODUCTIVE EVENTS IN THE COW

S. M. Omran and J. S. Boyd

*University of Glasgow Veterinary School*

The normal cycle of events occurring in the bovine reproductive tract was followed using B-mode two-dimensional real-time ultrasound examination. Initially, specimens obtained from the abattoir were examined ultrasonically in a water bath and photographic records made of any significant structures. The specimens were deep frozen and then sectioned to produce visual planes which resembled the ultrasound images This procedure was carried out in both pregnant and non-pregnant uteri so that images of the ovary, the uterus and the fetus at varying stages of the oestrus cycle and gestation were obtained This assisted in training the operator to interpret the scanning images. Subsequently, normal cows were examined at varying stages of the reproductive cycle using a rectal ultrasound probe and the images thus recorded demonstrated cyclic changes occurring in the ovaries, uterus and cervix. Further use of the rectal probe allowed normal pregnancies to be monitored and measurements taken of the developments in the fetal structures. These recordings were of particular benefit as known recorded mating dates were available. In a small number of live clinical cases where reproductive disorders were suspected, ultrasonic examination was carried out per rectum. When the animals came to post-mortem examination the ultrasound images could be related to the pathological findings detected at necropsy

## HOME-MADE ANTHROPOMORPHIC PHANTOMS

J. Dunnicliffe and M. F. Docker

*Birmingham Maternity Hospital*

A method for the construction of anthropomorphic tissue-equivalent phantoms for use in obstetric ultrasound training is described These phantoms are both relatively cheap and simple to make within the ultrasound department. A tissue-equivalent rubbery solid material can be formed by the addition of gelatine powder to a 10% methylated spirit and 90% water mixture. The attenuation is controlled by adding various concentrations of graphite powder. Methods of containing this material, in order to simulate tissue structures, such as the fetus, ovaries and bladder, are described. Materials such as wires and plastic tubes may be used to simulate fetal bones and blood vessels. The ultrasound phantom is contained within an air-tight box in order to prevent drying out of the gel material, thus making it suitable for long-term use

## A 10-YEAR STUDY OF FETAL GROWTH IN DIABETIC PREGNANCY

Jan Fog Pedersen and Lars Mølsted-Pedersen

*Ultrasound Laboratory, Glostrup Hospital and Department of Obstetrics and Gynaecology, Rigshospitalet, University of Copenhagen, Denmark*

More than 150 insulin-dependent diabetic pregnancies were followed by ultrasound scanning from early pregnancy until delivery. Fetal growth was analysed by means of the Rosavik formula As judged by the CRL, most fetuses were smaller than normal in early pregnancy This early growth delay was related to a poorer metabolic compensation The growth of the BPD did not deviate from normal, provided age was corrected for the early growth delay Earlier reports of a smaller-than-normal BPD in diabetic pregnancies are most likely explained by an undetected early growth delay in these studies. The abdominal circumference became larger than normal as early as Week 24, which, probably for the same reason, is earlier than reported in previous studies Among the first 99 babies in the study nine were malformed and seven were smaller than normal in early pregnancy. A follow-up study at 4 years of age revealed another three severely malformed infants They had also been smaller than normal in early pregnancy. This theoretically very interesting strong association between fetal malformation and early growth delay is of minor practical significance, because the number of malformed babies of diabetic women has decreased dramatically.

## COMPUTER-CONTROLLED IMAGING

S D. Pye, S. R. Wild and W. N. McDicken

*Departments of Medical Physics and Medical Engineering and Radiology, Western General Hospital, Edinburgh*

A new computer-controlled gain compensation system has been developed and is being tested clinically in obstetric and abdominal ultrasound Pairs of images are presented, one image of each pair having been produced using manually set gain compensation and the other using computer-controlled gain. The observer is left to judge the quality of the images before uncovering the text which indicates how each image was obtained

BIR Bulletin

June 1987

# After Chernobyl

By Richard F. Mould

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(*Received March 1987*)

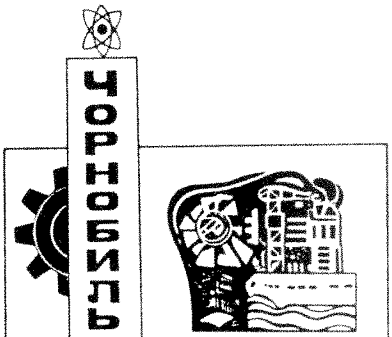
"Now, what I want is FACTS": Thomas Gradgrind in *Hard Times* by Charles Dickens (1812–1870)

Every aspect of the Chernobyl accident cannot be included in the space of a few pages and since the cause of the accident (mainly human error but with design faults contributing) has been described in many publications, as have the effects of the fallout on the food chain, this short review does not include these topics. An assessment of the number of excess cancer deaths due to the Chernobyl accident has also been excluded, for the good reason that accurate predictions are not yet available. "After Chernobyl" is therefore a factual account of interesting information on the evacuation and relocation of the population within a 30 km zone around the power plant, of decontamination efforts, of the entombment of the reactor (termed colloquially "the Sarcophagus", a title used by the Science Correspondent of *Pravda*, Vladimir Gubaryev, for the play widely performed in the Soviet Union and which in April–June 1987 was a Royal Shakespeare Company production at the Barbican Theatre in the City of London), and of the heroic firemen of Chernobyl, not all of whom survived.

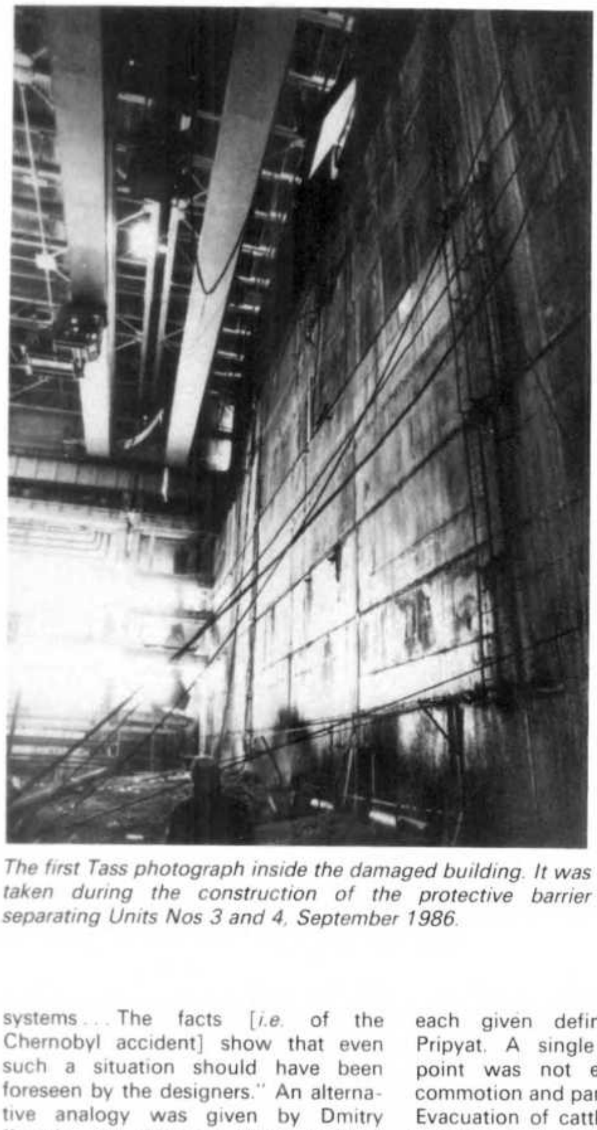
Much of the information is contained in my book *Chernobyl—The Real Story* (Pergamon Books Ltd, Oxford, 1987), which includes more than 100 photographs from sources such as the International Atomic Energy Agency (IAEA), Tass, Novosti, *Pravda*, *Izvestia*, Associated Press and miscellaneous photographic agencies. I am particularly indebted to Mrs Ludmilla Pachomova, the Photographic Librarian of the London office of Tass, for most of the illustrations in this review. Also, without the encouragement and assistance of friends and colleagues at IAEA and the World Health Organisation (WHO), and in many countries, this work would have been impossible. In particular, the opportunity to attend the IAEA Post-Accident Review Meeting in Vienna, August 25–29, 1986, gave me an excellent start, since as well as obtaining relevant papers from the USSR, I was also able to tape-record 13 hours of this meeting, including several hours of question and answer sessions which were not published by the IAEA as transcripts of the meeting and therefore represent a valuable and rare record of Soviet responses.

### *Explosion*

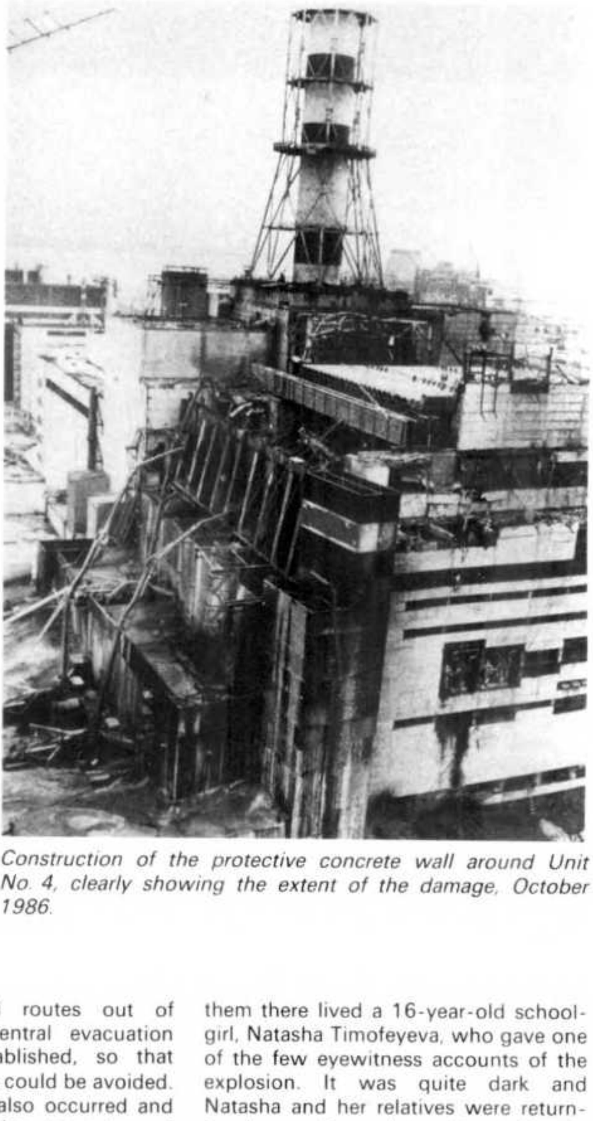
The steam explosion and outbreak of fire occurred at Unit No. 4 of the Chernobyl nuclear power plant at 01.23.48 on April 26, 1986. In a summary analogy of the accident Valeri Legasov, the USSR delegation leader at the IAEA Post-Accident Review Meeting, described the events leading up to the disaster as follows: "Imagine personnel of a 'plane which is flying very high. Whilst flying they begin testing the 'plane, opening the doors of the 'plane, shutting off various



*Entrance sign to the Chernobyl nuclear power plant, drawn from a photograph in* Izvestia, *May 19, 1986.*



*The first Tass photograph inside the damaged building. It was taken during the construction of the protective barrier separating Units Nos 3 and 4, September 1986.*



*Construction of the protective concrete wall around Unit No. 4, clearly showing the extent of the damage, October 1986.*

systems ... The facts [*i.e.* of the Chernobyl accident] show that even such a situation should have been foreseen by the designers." An alternative analogy was given by Dmitry Kazutin, the *Moscow News* political observer as "A peasant won't cross himself until he's hit by a thunderbolt" and he suggested that this Russian saying was probably coined even before the time of Tsar Peter the Great!

### *Evacuation*

The evacuation of Pripyat, the satellite town (population 49 000) for the power-plant workers, was announced at 14.00 hours on April 27 and with people allowed to take only the bare essentials, the entire evacuation took only two hours and 45 minutes. Militia forces organised checkpoints, roadblocks, cordons and control points and 1100 buses were used. Five main evacuation sectors were defined, with each given defined routes out of Pripyat. A single central evacuation point was not established, so that commotion and panic could be avoided. Evacuation of cattle also occurred and this was achieved using some tens of thousands of open trucks.

The eventual total number of evacuees from a zone of 30 km around the Chernobyl plant was 135 000, including the Pripyat population (3 km from the plant) and 12 000 from the town of Chernobyl (15 km from the plant). The farming communities in the small villages within the 30 km zone would have been more of an organisational problem in the evacuation, not to mention a psychological problem having to leave land they had farmed for many years. A typical village was Chamkov, in the Gomel region of Byelorussia, 6 km from the power plant on the opposite side of the river Pripyat. It contains only 55 houses and in one of them there lived a 16-year-old schoolgirl, Natasha Timofeyeva, who gave one of the few eyewitness accounts of the explosion. It was quite dark and Natasha and her relatives were returning home after a late visit to friends, when she saw "a bright flash over the fourth, most distant chimney of the power plant." (In all, the total population evacuated from the Byelorussian villages was 13 200.)

### *New towns and villages*

The new towns and villages were planned and built very quickly. One in the Gomel region, completed by October 1986, contained in its first construction stage 4000 houses, and in the second stage schools, laundries, hospitals, kindergartens, canteens, clubs, trade centres, post offices (many postmen were evacuated with their local population and retained their old job in their new environment) and other

*Part of the 6000 tonnes of metal structures which, with 400 000 tonnes of concrete, formed the sarcophagus.*

*Helicopter spraying decontaminants in the area of the power plant. Helicopters were earlier used on "bombing missions" to put out the fire in the reactor core by smothering it with silicates, dolomite, sand and other materials.*

*The old and the new in Kiev, the Soviet Union's third largest city.*

facilities. Construction of this particular town was carried on 24 hours a day in shifts, employing 3000 workers.

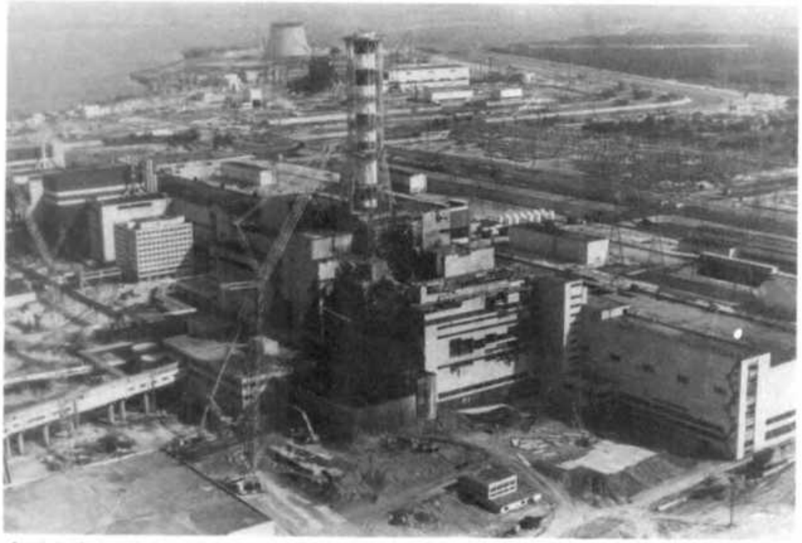
Sites for farming communities were also necessary. For instance, in the Makarov district of the Kiev region, 150 houses were built for the Chervone Polessya collective farm workers. In each house were placed two beds and a cot, by the builders, and food gifts of two bags of potatoes, cereals, jars of pickled cucumbers, and tomatoes. Each household was allotted 10 hens and a pigeon loft was placed near one house. In this Kiev region 52 new townships were built in the short period of six to eight weeks.

*Decontamination and limitation of the spread of radioactivity*

The problems of a very rapid decontamination of the plant and surrounding areas (buildings, transport, roads, soil, forests and other vegetation) in the 30 km zone were insurmountable. Nevertheless, as the IAEA Post-Accident Review Meeting heard, an impressive decontamination and containment operation was put into action. Special roads were constructed and a pontoon bridge was built to span the river Pripyat, all working vehicles were given strict operating limits to avoid spread of contamination, embankments were set up around the power plant, a protective wall was built alongside the Pripyat to prevent radioactive contamination in the case of torrential rainfall, a protective wall (built to an underground depth of 30 m) was erected to prevent the outflow of ground water from the plant area, specially trained soldiers from the Chemical Defence Force decontaminated (using a liquid polymase) homes and other buildings, to mention only a few of the procedures adopted.

One of the unknown factors in the operation was the future wind and rainfall patterns, which could not only obstruct current decontamination work but could recontaminate previously cleaned sites. The possibility of forest fires was also a concern. Additionally, a major concern was the possibility of contamination of the river Dnieper and the water supply to the Soviet Union's third largest city, Kiev, with a population of two and a half million. Professor V. I. Trefilkov, Vice-Chairman of the Ukrainian Academy of Sciences, described this concern and stated that in the first few days after the accident, measures were taken to provide alternative water supplies for Kiev and that 400 wells were bored to replace the water supply normally taken from the Dnieper. As part of the scheme to provide clean water, a pump-ship, the *Rosa-300*, was moored in the river Desna and two emergency water supply mains, each 6 km in length, were built. These pipelines had to be thrown over 18 obstacles including rivers, bridges, tunnels and roads.

*Remote-controlled bulldozer used for earth moving, June 1986. This is a giant, 19-tonne caterpillar bulldozer with a CTZ trademark for the Chelyabinsk Tractor Works. It was delivered from Chelyabinsk to Kiev on board a specially modified Ilyushin-76 jumbo jet, and then fitted out with sophisticated electronic equipment at institutes in Kiev. The operator views surroundings through a narrow slit in an armoured vehicle several dozen metres distant. In* Pravda, *October 10, it was reported that at the territory of the plant, soil was removed to a depth of 30 cm, and that it had taken two months to decontaminate the plant.*



*Aerial view of the power-plant site, September 1986.*

*Radiation monitoring checkpoint at the boundary of the 30 km zone, May 1986.*

*New housing for evacuees in the village of Pologiya Verguny in the Cherkassy region of the Ukraine, August 1986.*

The population was given strict instructions not to enter the 30 km zone and one order concerning food stated that "people such as anglers and those who like to gather mushrooms and berries are warned that the 30 km zone has been sealed off and they should not try and penetrate it."

*Decontamination of the plant area*

Decontamination of the plant area was undertaken in the following sequence. (1) Removal of refuse and contaminated equipment from the site. (2) Decontamination of roofs and outer surfaces of buildings—sometimes pastes were put on walls so that they enabled a quick-drying film to be formed, which when peeled off had radioactive particles sticking to it. (3) Removal of a 5–10 cm layer of soil and its transfer in containers to the waste disposal dump at the excavated site of a planned new unit, No. 5. (4) Laying, if necessary, concrete slabs on the soil or filling with clean earth. (5) Coating of the slabs and of the non-concrete area with film-forming compounds. The work-rate of the decontamination teams was such that surfaces were cleaned at a rate of 15 000–35 000 m² per 24 hours.

*Entombment of the reactor*

Between April 27 and May 10, about 5000 tonnes of boron compounds, dolomite, sand, clay and lead were dropped from helicopters to cover the damaged reactor. The first "crater bombing missions" by the air force were the most difficult; on the first day 93 missions were flown and on the second day 186. Overflying speed was 140 km per hour and the accuracy of the drop was aided by instructions from a monitoring plane equipped with instruments.

An underground bunker was dug under one of the site buildings 600 m from Unit No. 4 and this acted as the control outpost for the co-ordination of operations. A special group of coal miners from Tula and the Donets basin were drafted in for the emergency to build a "cooling slab" (a reinforced concrete slab incorporating a heat exchanger) under the reactor of Unit No. 4. Limited shifts of three hours were set for the miners, because of conditions, but the entire operation was still completed by June 24. It involved a workforce of 400. The first 6 m was solid sandstone and the tunnelling rate was 60 cm of sandstone rock per hour. The tunnel, which is encased in reinforced concrete, is 168 m long and

1.8 m in diameter. The final 5–6 m had to be worked manually. Service lines and rails for buggies were laid inside the tunnel and 13 small galleries were built where riggers could assemble what were called "dampers" (devices for cooling the foundations of the reactor).

The engineering plans for the sarcophagus of Unit No. 4 were as follows: (1) outer protective walls along the perimeter; (2) inner concrete partition walls in the turbine hall between Units Nos 3 and 4 and in other places, including the site of the debris by the tank room of the emergency cooling system; (3) a metal partition wall in the turbine hall between Units Nos 2 and 3; and (4) a protective roof over the turbine hall.

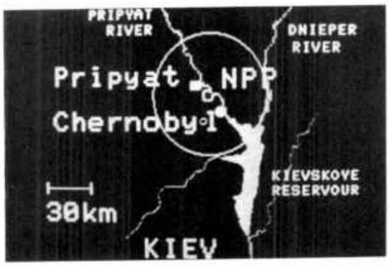
The final entombment occurred in mid-November, somewhat delayed because of a shortage of concrete. This shortage was perhaps not very surprising since, by September 15, more than 160 000 m³ of concrete had already been poured into shielding structures, which by then had reached the height of 41 m. The concrete wall around the perimeter of the Chernobyl power plant was really a trench 60 cm wide and 30–35 m deep. The total concrete used in the sarcophagus was some 400 000 tonnes.

*Medical response: the first 10 hours*

The explosion occurred at 01.23.48 hours and at 01.30 the three staff on duty at the power plant site medical centre were alerted and the Moscow emergency centre notified using the code words "NUCLEAR", "RADIOACTIVITY" and "FIRE". At 01.45 two specialised teams of medical staff left Pripyat and 115 beds were made available in regional hospitals. By 02.10 when the main fires on the turbine generator machine hall roof had been extinguished, the first 29 casualties had been admitted to hospital. At 03.00 potassium iodate tablets were distributed to all power-plant workers and hospital patients. By 06.00 the number of people hospitalised had risen to 108 (a further 24 were also later admitted) and one person had died from severe thermal burns. Only five were to receive significant thermal burns and it was the beta radiation burns which were the prime cause of the fatalities. Special emergency teams of physicists, dermatologists, radiologists and clinicians were alerted in Moscow at 06.40 and flew to Kiev at 11.00.

*The author and Lieutenant-Colonel Leonid Telyatnikov, March 6, 1987.*

*Drillers help themselves to the first mouthfuls of water from an artesian well they have just sunk near Kiev.*



*Map of the area around the nuclear power plant, as presented by the USSR delegation at the IAEA Post-Accident Review Meeting.*

*Decontamination of apartment blocks which once housed the power-plant workers in Pripyat, May 1986.*

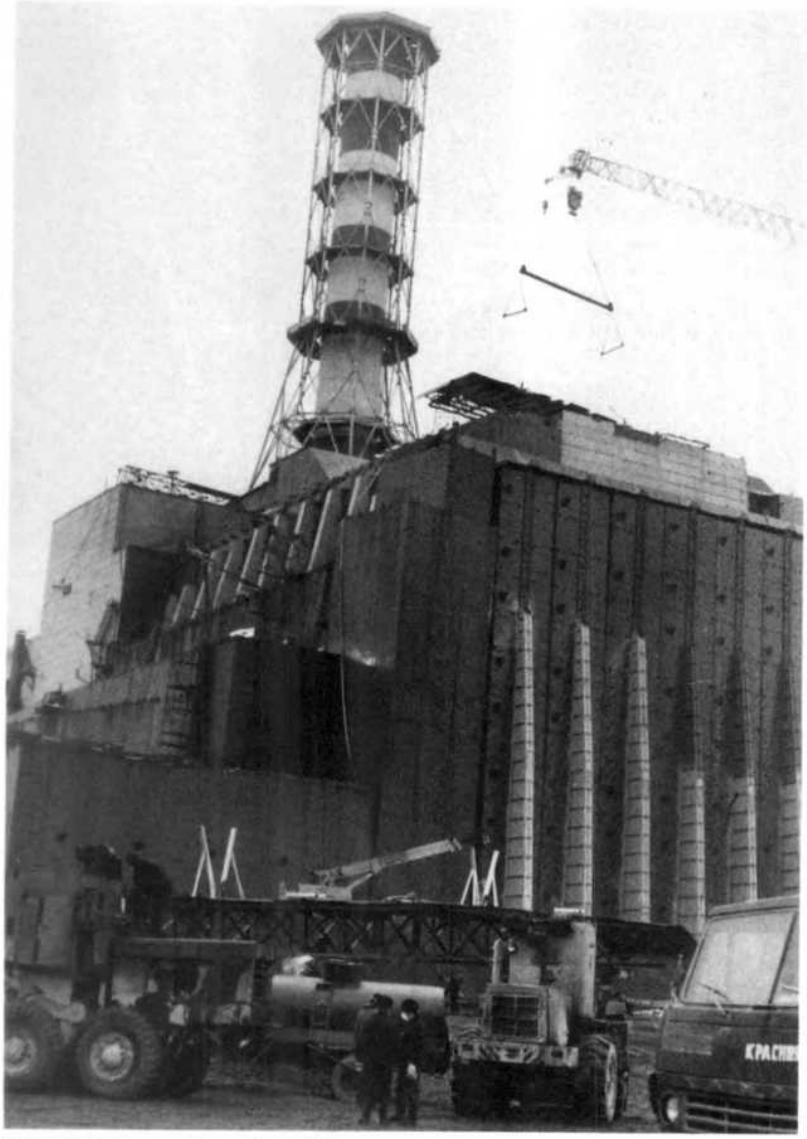
*Decontamination of areas of forest and other vegetation, May 1986.*

The on-site medical teams quickly had to establish broad clinical criteria to determine who should be evacuated, and this was achieved by defining three groups: (1) the very sick who needed immediate evacuation; (2) the not very sick; and (3) those who had no symptoms of radiation sickness. Group 1 included those who suffered the onset of vomiting during the first half hour or so of work, diarrhoea, temperature increase, emissions from mucous membranes, and hyperaemia of the skin, particularly on open surfaces. One hundred and thirty persons were found to be in Group 1 and 129 were later sent to specialised hospitals in Moscow and Kiev. Here, in addition to treatment, they underwent many tests including thyroid counting for radioactive iodine, gamma-ray spectrometry using whole-body counters, urine analysis for radioactive content and biochemical and metabolic studies.

*Radiation sickness*

Up to May 10, several hundred thousand people were medically examined, including the taking of blood tests, and 299 were diagnosed with some degree (first to fourth) of radiation sickness. Two hundred and three were ultimately found to have second to fourth degree radiation sickness.

Classification was according to the radiation dose received; first degree, less than 100 rad; second degree, 100–400 rad; third degree, 400–600 rad; fourth degree, 600–1600 rad. Of the 29 deaths reported by the end of August 1986, 21 were fourth degree, seven were third degree and only one was second degree. The time scale of



*The Sarcophagus, December 1986.*

these deaths was 9–28 days post-accident for fourth degree and 14–49 days for third degree radiation sickness.

*Radiation burns*

Most people who died experienced severe radiation burns covering more than 40% of their total body area and of the 56 patients under the charge of Professor Angelina Guskova at the specialist Moscow Hospital No. 6, 48 exhibited burns within three weeks, including some within several hours. Some of this group tragically experienced a second wave of radiation burns which covered new portions of their skin and extensions to earlier skin damage. In 20 cases, the unfortunate victims also suffered from a virus infection of the beta radiation burnt skin, causing the most terrible pain.

*Bone marrow transplants*

The results from transplants (13 bone marrow and six fetal-liver) were not very successful and in August 1986 Professor Guskova concluded that "for radiation accidents the proportion of patients in whom transplantation of allogenic bone marrow is absolutely indicated for beneficial treatment is very small" and that in some cases, the transplant "might even endanger life as a result of the higher risk of secondary disease developing."

*Rehabilitation of the Chernobyl firemen*

In the May 19, 1986 issue of *Izvestia*, the obituaries of the six firemen who died were given with eyewitness accounts of some of their colleagues. Some were able to tolerate the conditions for only a relatively short period of 15–20 minutes, with melted bitumen on the roof making their boots as heavy as lead, and smoke and dust almost blinding them, in addition to the radiation hazard.

Many were young, as recorded by fireman Ivan Shavrei. "I went up onto the roof of the machine room, on the way we passed the kids from the Specialised Military Fire Brigade No. 6, they were in a bad way. We helped them to the fire ladder, then made our way towards the centre of the fire where we were to the end. After finishing the job [on the roof] we went back down, where the ambulance picked us up. We too were in a bad way."

The head of the Chernobyl power-plant fire brigade, Major (now Lieutenant-Colonel and Hero of the Soviet Union) Leonid Telyatnikov, was in London on March 6, 1987, where I was fortunate to be invited to interview him at the Soviet Embassy. He summarised his post-accident experience as "two months' treatment in hospital, one month rehabilitation, one to two months' health resort treatment at a sanatorium, two to three months of general medical checks and then by February, ready to resume fire duties."

*New radiological centre in Kiev*

A new radiological centre has been set up in Kiev, devoted to follow-up studies of the Chernobyl disaster. It consists of three research units: an Institute of Experimental Radiology, an Institute of Clinical Radiology and an Institute of Epidemiology & Prevention of Radiation Sickness. It is from this centre, and possibly from IAEA and WHO, that we can expect to receive the publication of results of on-going investigations of the effects of Chernobyl, for many years to come.

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*Watch out for the full papers from the one-day seminar "Nuclear Reactor Accidents: Preparedness and Medical Consequences" in a forthcoming issue of* BJR.

## A tribute to Professor Joseph S. Mitchell, F.R.S.

I would like to add a personal note to the many tributes which have been offered to the memory of Professor Joseph Mitchell. I do so as one who came to know Professor Mitchell late in life, but was then privileged to enjoy a close and fruitful collaboration with him for nearly seven years

Joseph Mitchell was a physician, a scientist, an academic, a practical man of business, a loving husband and father, and a caring, warm-hearted human being. I was privileged to observe all of these facets of this many-sided man. His scholarly achievements have been well documented, from his work before and during World War II (he was the first to suggest, in 1946, the use of cobalt 60 in radiotherapy) to his recent researches in which he came close to achieving a lifelong ambition to develop a practical radiopharmaceutical which selectively destroys cancer cells from within. Yet, in spite of the written record, Professor Mitchell's many contributions to cancer therapy tend to be underestimated because he was a modest man who shunned the limelight

Perhaps the two characteristics of Joseph Mitchell's personality and work particularly worthy of note were his breadth of knowledge, from minor details of anatomy to subtle aspects of nuclear physics, and his concern for other people He was always anxious that anyone who worked with him, in any capacity, should be well looked after and receive proper recognition.

No tribute to Joseph Mitchell would be complete without mentioning his wife of so many years, Mary. Mary was herself a physician and social worker of no mean stature, but she will also be remembered as one who did more than any other individual to encourage, support and contribute to her husband's work Mary Mitchell was as near a saint as any of us are likely to encounter in a lifetime Her death in 1983 was a devastating blow to Joseph and, indeed, to all who knew and loved her.

With the passing of Joseph Mitchell, radiotherapy has lost a pioneer and leader, Cambridge an outstanding scholar, and humanity a man of deep compassion and understanding. Our sincere sympathies are extended to his son Kit and his family, and to his daughter Janet

MONTAGUE COHEN

# BIR calendar events

*Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).*

*The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members*

**Dementia**
October 15, 1987

**Chemical Modification of Radiation Effects—Experimental and Clinical**
November 13, 1987

**New Radiopharmaceuticals and Their Clinical Applications**
November 27, 1987
Scientific Societies, London W1
Organised by the Nuclear Medicine Subcommittee.

**British Institute of Radiology 46th Annual Congress**
*incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting and in collaboration with the Scottish Radiological Society*

### Radiology '88

Glasgow May 23–25, 1988

Glasgow will be the first in a series of back-to-back meetings with the Annual Conference of the College of Radiographers. The technical exhibition will span both meetings and be the manufacturers' showcase in 1988.

The place. the brand new Scottish Exhibition and Conference Centre

Radiology '88 will cover all aspects of radiology: X-ray diagnosis, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines

Proffered papers and posters are invited. closing date November 30 1987

# Library news

**The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)**

*The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a m –5 p.m. (Tel. 01-580 4085).*

*The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the* Bulletin. *Most books (excepting the historical collection) are available on loan.*

*There is an agreement which allows BIR members limited use of the RSM Library for reference purposes Members should apply to the BIR Librarian for a visitor's card*

**Recent additions to the Library**

Bleehen, N. M (Ed ). Investigational techniques in oncology. 1987
Deeley, T. J.: Wilhelm Conrad Rontgen, his life and the new kind of rays 1986
Gough, M H , Gear, M W L & Daar, A S . Plain X-ray diagnosis of the acute abdomen 2nd edit. 1986
Heiken, J P , et al (Eds) Manual of clinical magnetic resonance imaging 1986
NRPB. National survey of doses to patients undergoing a selection of routine X-ray examinations in English hospitals. 1986
Phelps, M E., Mazziotta, J C & Schelbert, H R (Eds): Positron emission tomography and autoradiography principles and applications for the brain and heart. 1986
Sanders, R. C & Hill, M C (Eds). Ultrasound annual 1985
Wicke, L Atlas of radiologic anatomy 4th English edit. 1987
New journal
Journal of interventional radiology

**The BIR Nycomed Scandinavian Scholarships 1988**

Applications should be submitted by July 31, 1987, and interviews will take place in September

For further information please write to: The General Secretary, The British Institute of Radiology, 36 Portland Place, London W1N 4AT.

# Meetings and courses

*As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge. any additional information will be charged at £1 75 per printed line, per insertion Please contact the Managing Editor.*

**Ninth International Conference on the Use of Computers in Radiation Therapy**
June 22–25, 1987
The Hague
Further details. Organisation IX ICCR, Ir P H van der Giessen, Dr. Bernard Verbeeten Institute, P.O. Box 90120, 5000 LA Tilburg, The Netherlands, (Tel. 013 655 726).

**The Cambridge Meeting on Frontiers in Ultrasound**
July 3–4, 1987
King's College, Cambridge
Further details· Dr John Tudor, Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ

**Blood Flow '87 (Techniques in blood flow measurement and their relevance to clinical diagnosis)**
July 7–8, 1987
University of Leeds
Further details Mr R. Price, Department of Medical Physics, Leeds General Infirmary, Leeds LS1 3EX

**1st Biennial Brachytherapy and Remote Afterloading Symposium and Workshop**
September 14–16, 1987
St Louis, Missouri, USA
Further details Carlos A Perez, M D, Symposium Chairman, Director, Radiation Oncology Center, Mallinckrodt Institute of Radiology, 4511 Forest Park Boulevard, Suite 411, St Louis, Missouri 63108, USA (Tel 314-362 3497).

**Organ Imaging Review**
September 14–18, 1987
Toronto, Canada
Further details Edward E. Kassel, M.D., Program Director, Department of Radiology, University of Toronto, Room 127 Fitzgerald Building, Faculty of Medicine, Toronto, Ontario, Canada M5S 1A8 (Tel. 416-978 6801).

**Intra-operative Ultrasonography**
September 18–19, 1987
Paris, France
Further details Convergences, 16 rue Jean Jacques Rousseau, 75001 Paris, France.

**4th International Symposium on Diagnostic Imaging**
October 19–23, 1987
Barcelona, Spain
Director Dr Carlos Sanpons, Barcelona, Spain
Co-director: Dr Manuel Viamonte, Jr Miami Beach, Fla., USA
Sponsored by Mount Sinai Medical Center, Miami Beach, Fla, USA
Category I, Credit 36 hours
Subjects Sonography, Nuclear Medicine, CT, DSA, MRI, PET, etc
Official languages: Catalan, Spanish and English
Inscriptions. Centro Radiológico Computarizado de Barcelona, Tavern, 82, 08006 Barcelona, Spain
Fees Before October 1 $400 ($200 for residents)
After October 1: $500 ($250 for residents) (residents must have letter of the chief of their training programme)
Registration is limited to 400
Further details: Núria de Arana, c/o Centro Radiologico Computarizado de Barcelona, Tavern, 82, 08006 Barcelona, Spain.

**Principles and Practice of Radiotherapy**
October 26–29, 1987
Ljubljana, Yugoslavia
Further details. European School of Oncology, Via Venezian 1, 20133 Milan, Italy (Tel 02 235 923-266 4662).

**Residential Course: Integrated Management of Head and Neck Cancer**
November 5–9, 1987
Stoke Rochford Hall, Nr Grantham, Lincolnshire
Further details· Mr P J Bradley, Consultant ENT Surgeon/Head and Neck Oncologist, University Hospital, Queen's Medical Centre, Nottingham NG7 2UH (Tel 0602-410 679)

**6th Annual Christie Hospital Symposium: Current Controversies in Radiotherapy**
November 6–7, 1987
Manchester
Further details Dr B. Hancock, Consultant Radiotherapist, Christie Hospital, Wilmslow Road, Withington, Manchester M20 9BX.

**9th London Ultrasound Course**
November 9–13, 1987
Skyway Hotel, Hayes, Middlesex
Further details: Dr H B Meire, X-ray Department, King's College Hospital, Denmark Hill, London SE5 9RS

**9th Conference on Medical Physics**
December 10–12, 1987
Trivandrum, India
Further details. Dr A S Pradhan, Convener, Scientific Programme Committee, 9th Conference on Medical Physics, Division of Radiological Protection, Bhabha Atomic Research Centre, Bombay—400 085, India

**Monoclonal Antibodies in Oncology**
December 17–18, 1987
Bahia Blanca, Argentina
Further details. European School of Oncology, Via Venezian 1, 20133 Milan, Italy (Tel. 02 235 923-266 4662)

**7th International Congress of the International Radiation Protection Association: radiation protection practice**
April 10–17, 1988
Sydney, Australia
Further details IRPA 7 Secretariat, GPO Box 2609, Sydney, NSW 2001, Australia (Tel. 02-241 1478, Telex AA74845 "Consec", Cable "Convention" Sydney)

**5th International Symposium on the Planning of Radiological Departments**
April 20–23, 1988
Florence, Italy
Further details ISPRAD V Organizing Secretariat, CLAS Editoriale, Via Pace 8, 25122 Brescia, Italy.

**European Joint Committee on Radiopharmaceuticals 3rd Postgraduate Course on Radiopharmacy for Clinicians**
October 17–22, 1988
Stadtisches Klinikum Berlin Buch, DDR
Further details: Professor Dr H Deckart, Stadtisches Klinikum Berlin Buch, Nuklearmedizinische Klinik, DDR-1115 Berlin-Buch, Wiltbergstr. 50, Haus 144 or Professor Dr P H Cox, Dept of Nuclear Medicine R R T I, Postbus 5201, 3008 AE Rotterdam, The Netherlands.

# CHERNOBYL
## THE REAL STORY

**R F MOULD,** *Westminster Hospital, London, UK*

Written by an international expert in medical physics and cancer statistics, this book brings together, for the first time, a detailed description of the accident at Chernobyl with the most complete pictorial record ever compiled. The photographs include many never seen before in the West, giving the reader an unparalleled insight into the worst ever civil nuclear disaster. The book records the details behind the evacuation of the surrounding area, the entombment of the reactor and the decontamination of the environment, and describes the personal histories of those involved, including many of the firemen who were to lose their lives. It also outlines the degree of contamination of the surrounding countries and the response of the European governments and press to this environmental disaster.

For all those interested in the facts behind the disaster at Chernobyl.

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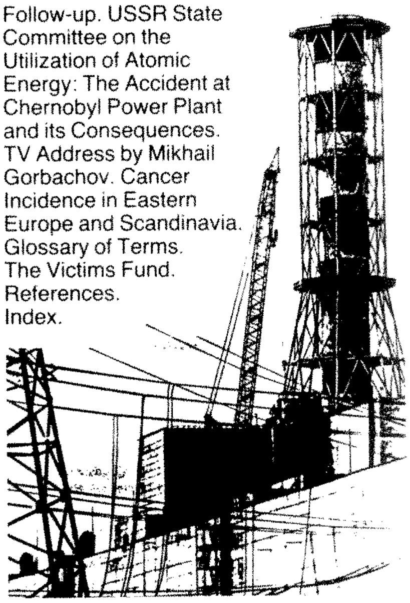

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# Clinical Radiology

*The Journal of the Royal College of Radiologists*

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*Clinical Radiology* is the journal of the Royal College of Radiologists, London and is published bimonthly. Each issue contains up to twenty original research papers from all over the world, supplemented by occasional review articles of interest to diagnostic radiologists, radiotherapists, oncologists and other medical practitioners.

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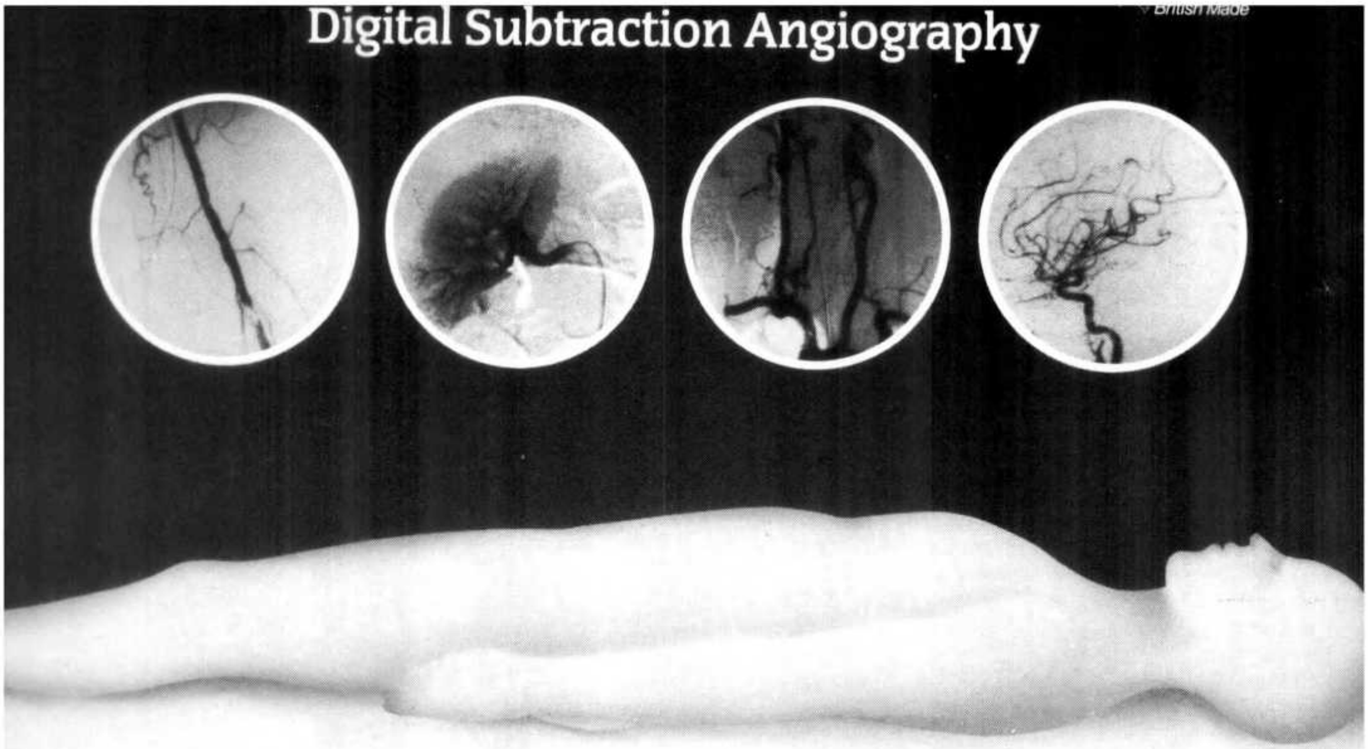

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Volume 60 Number 715
July 1987

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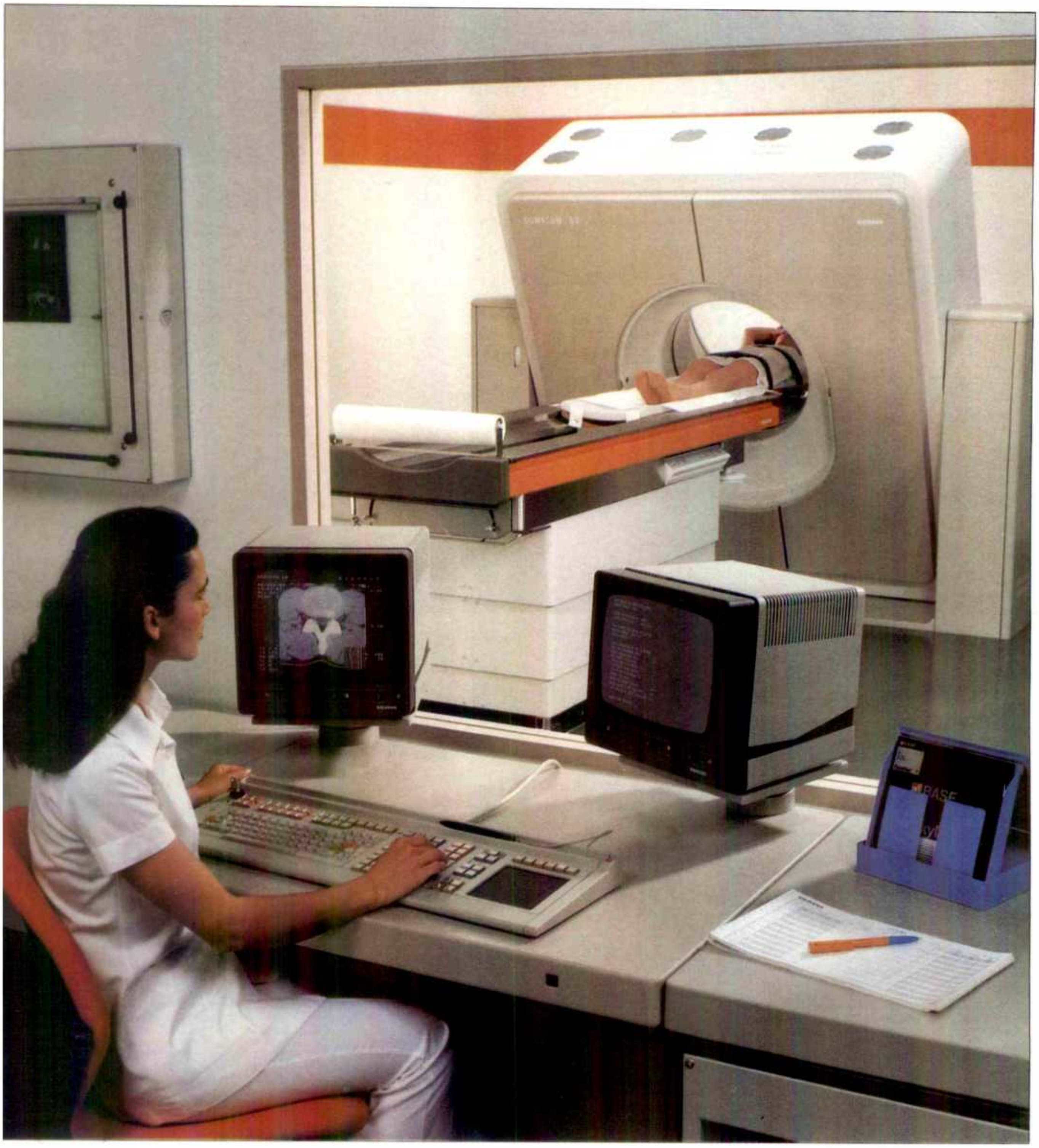

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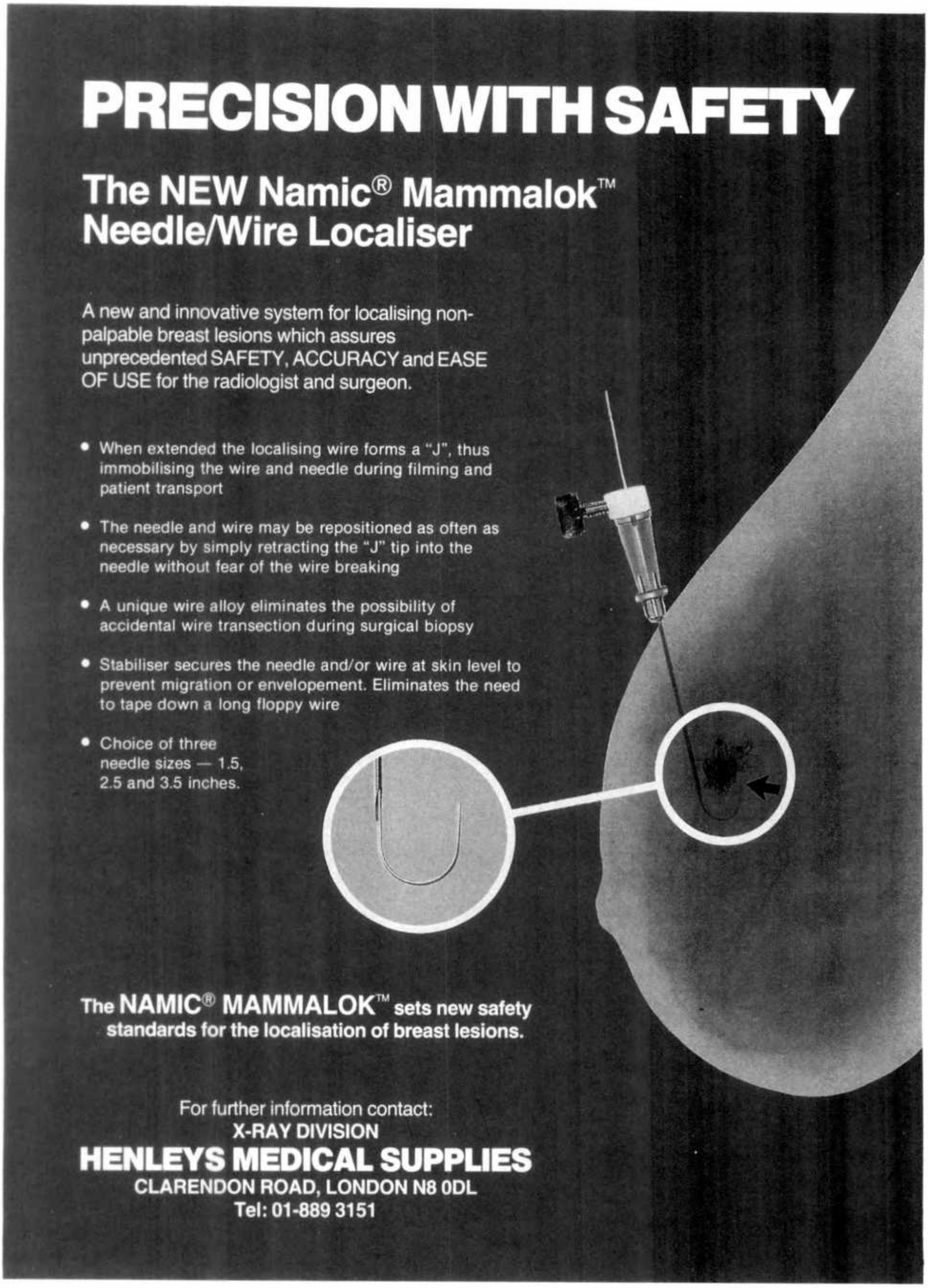

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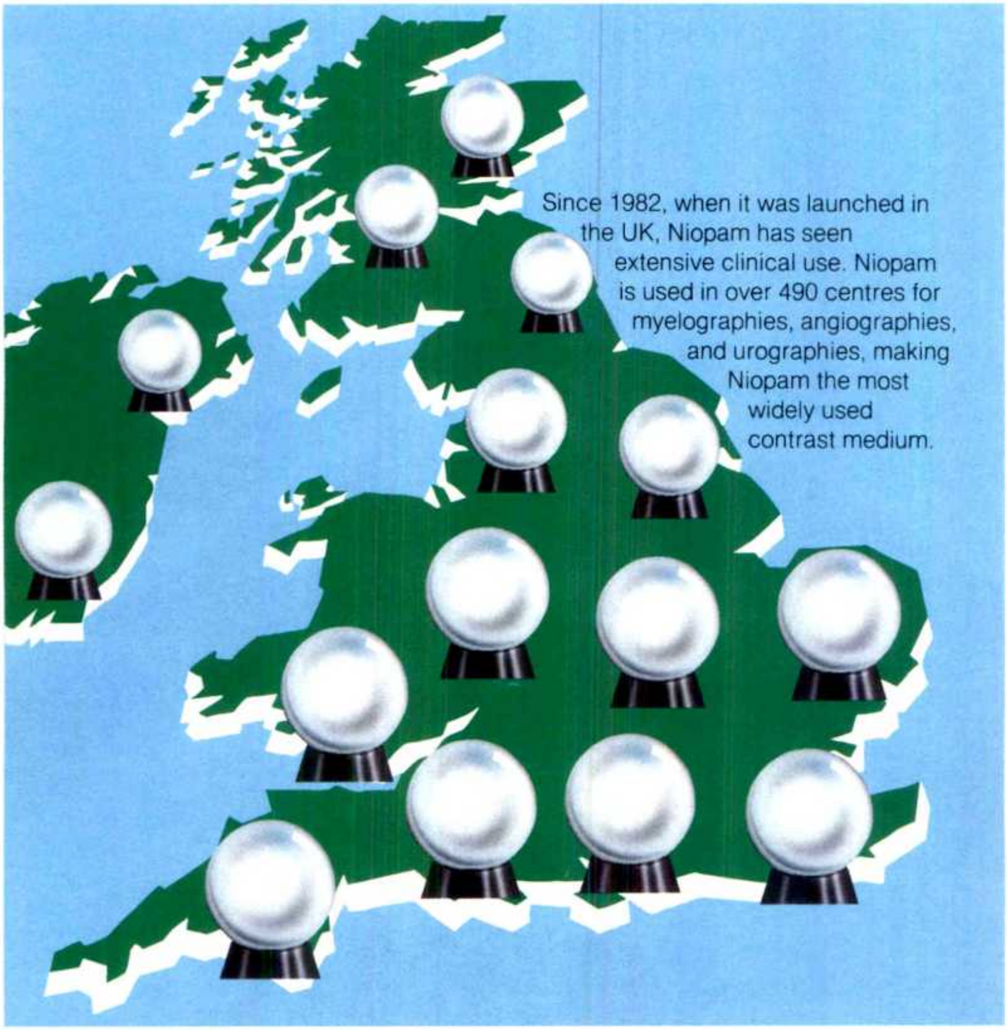
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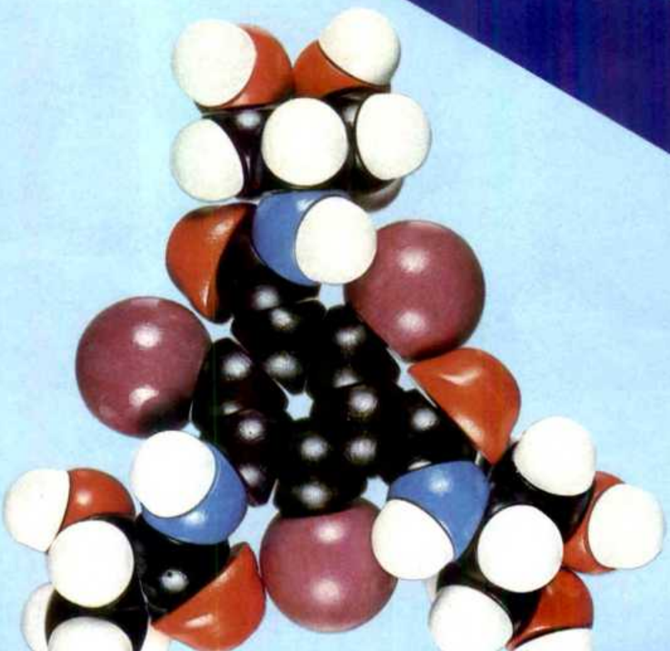

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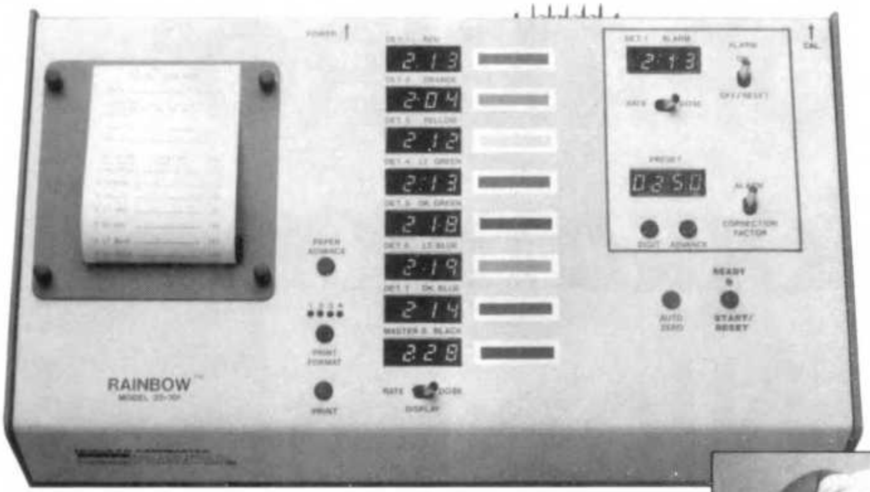

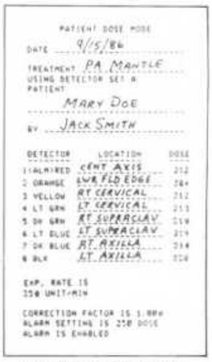

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4 LT GRN    LT CERVICAL
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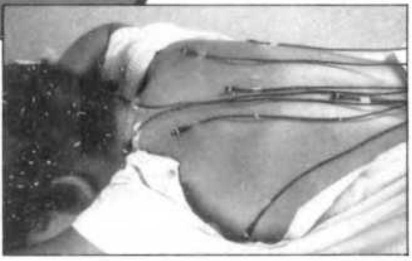

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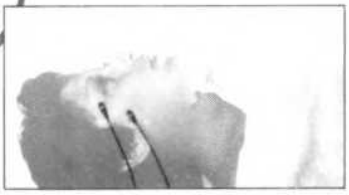

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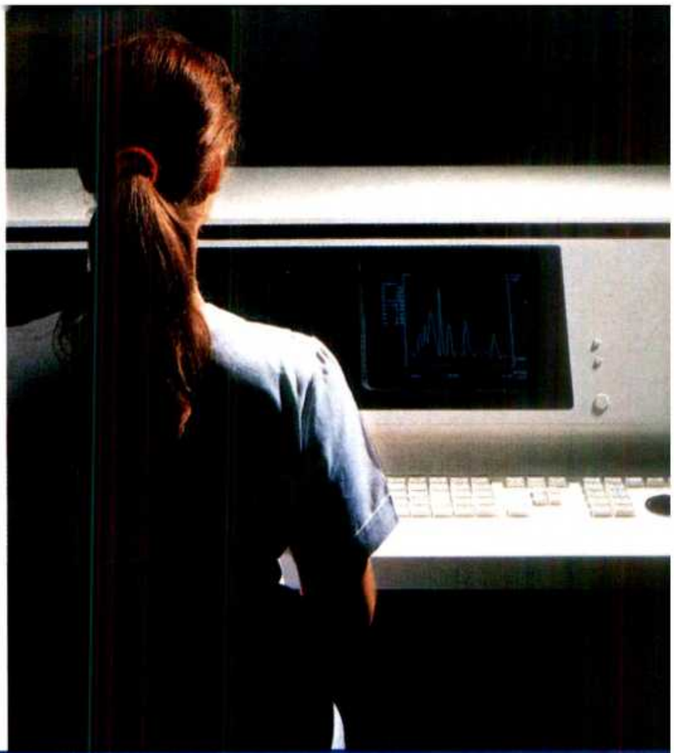

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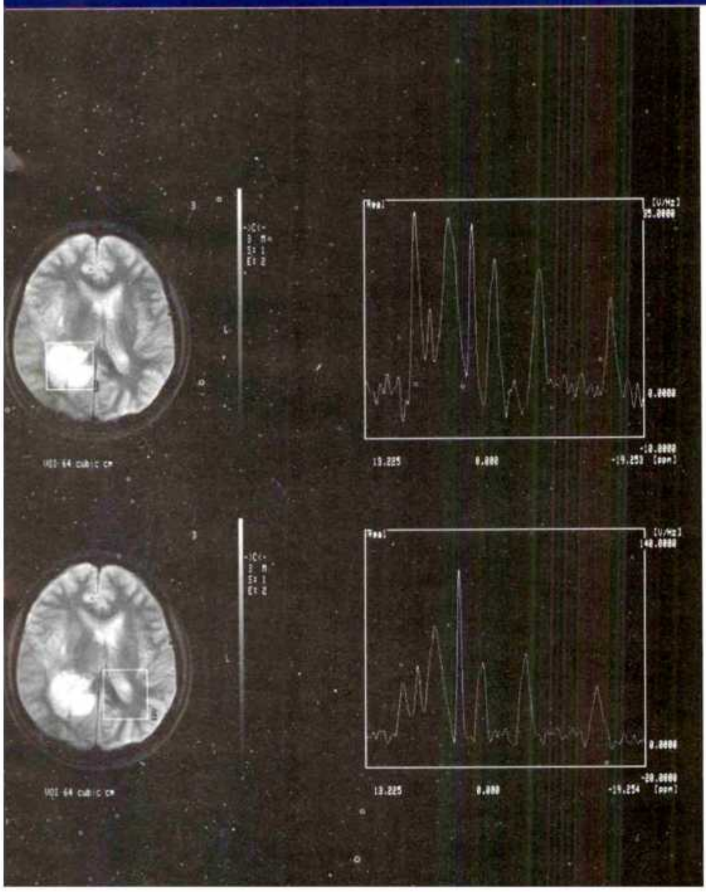

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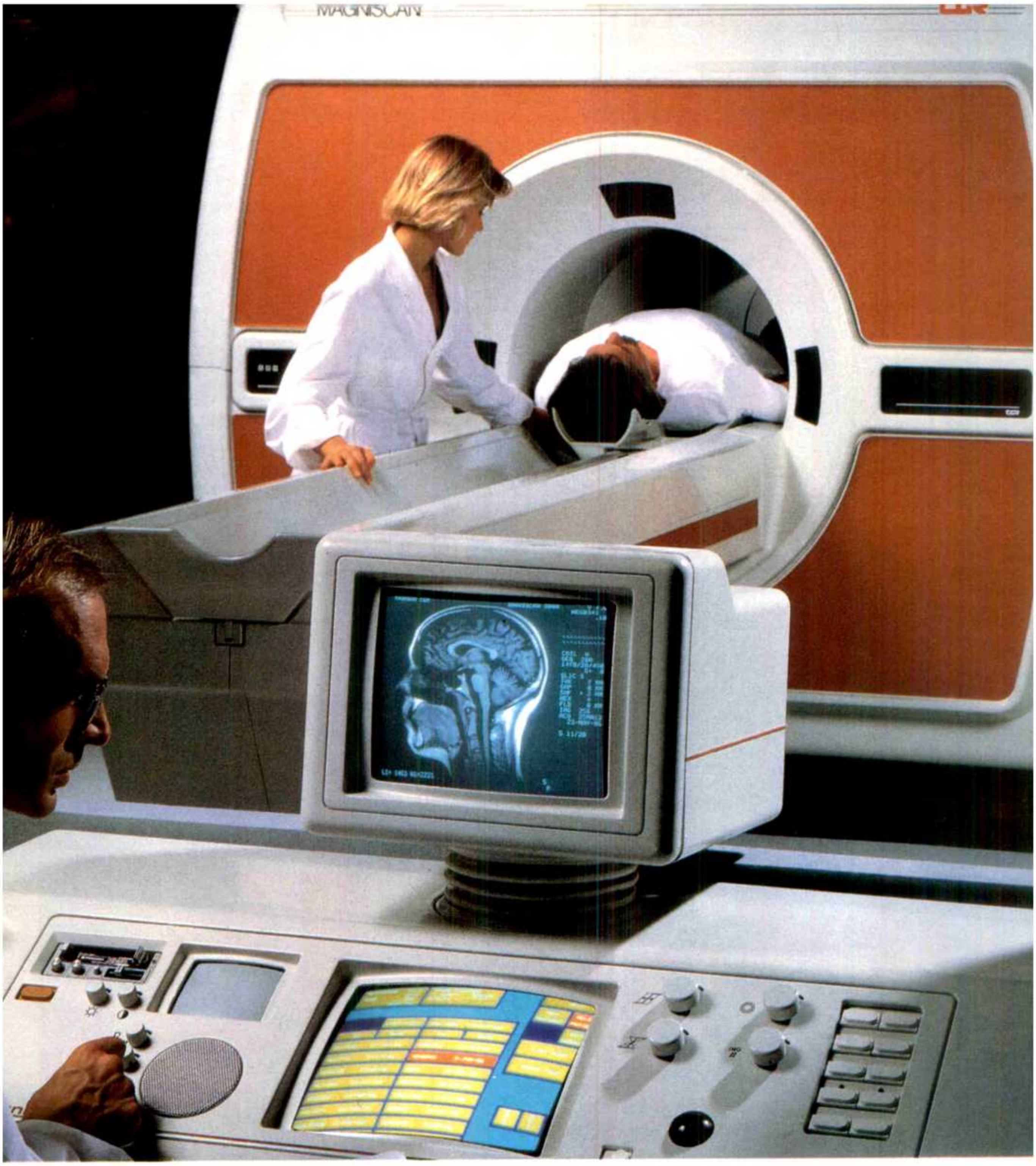

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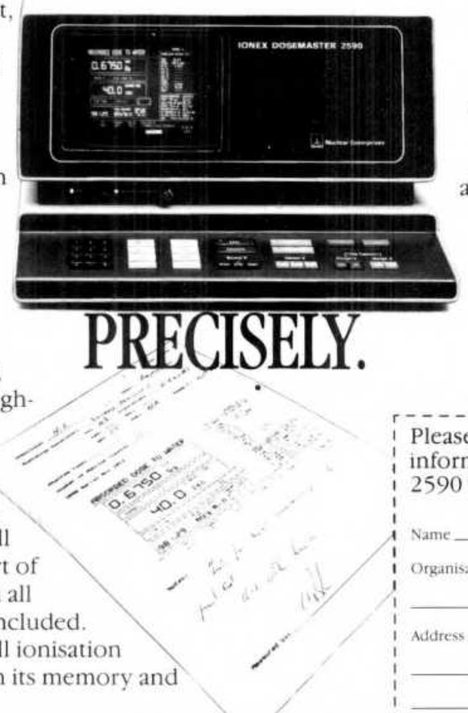

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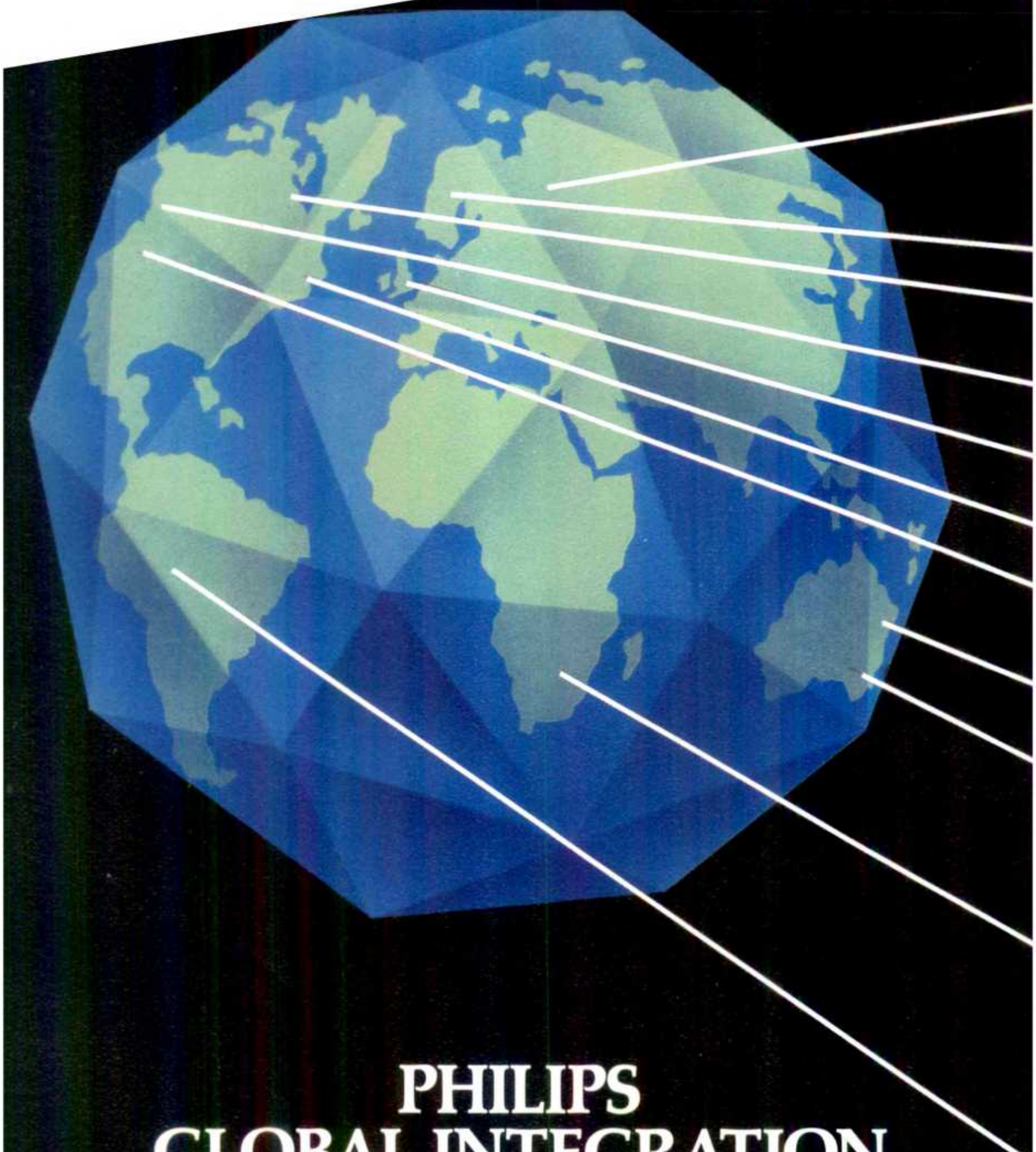

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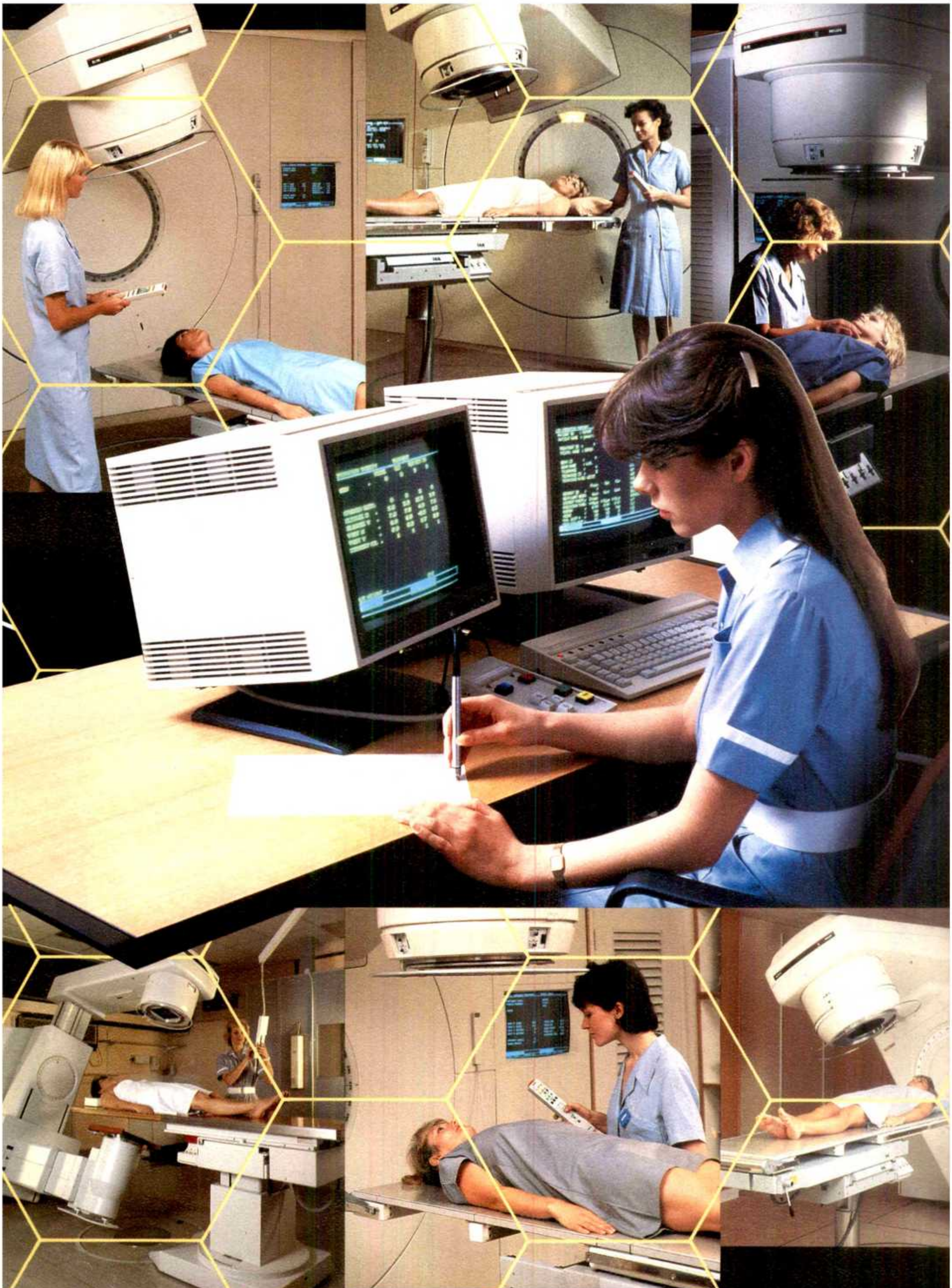

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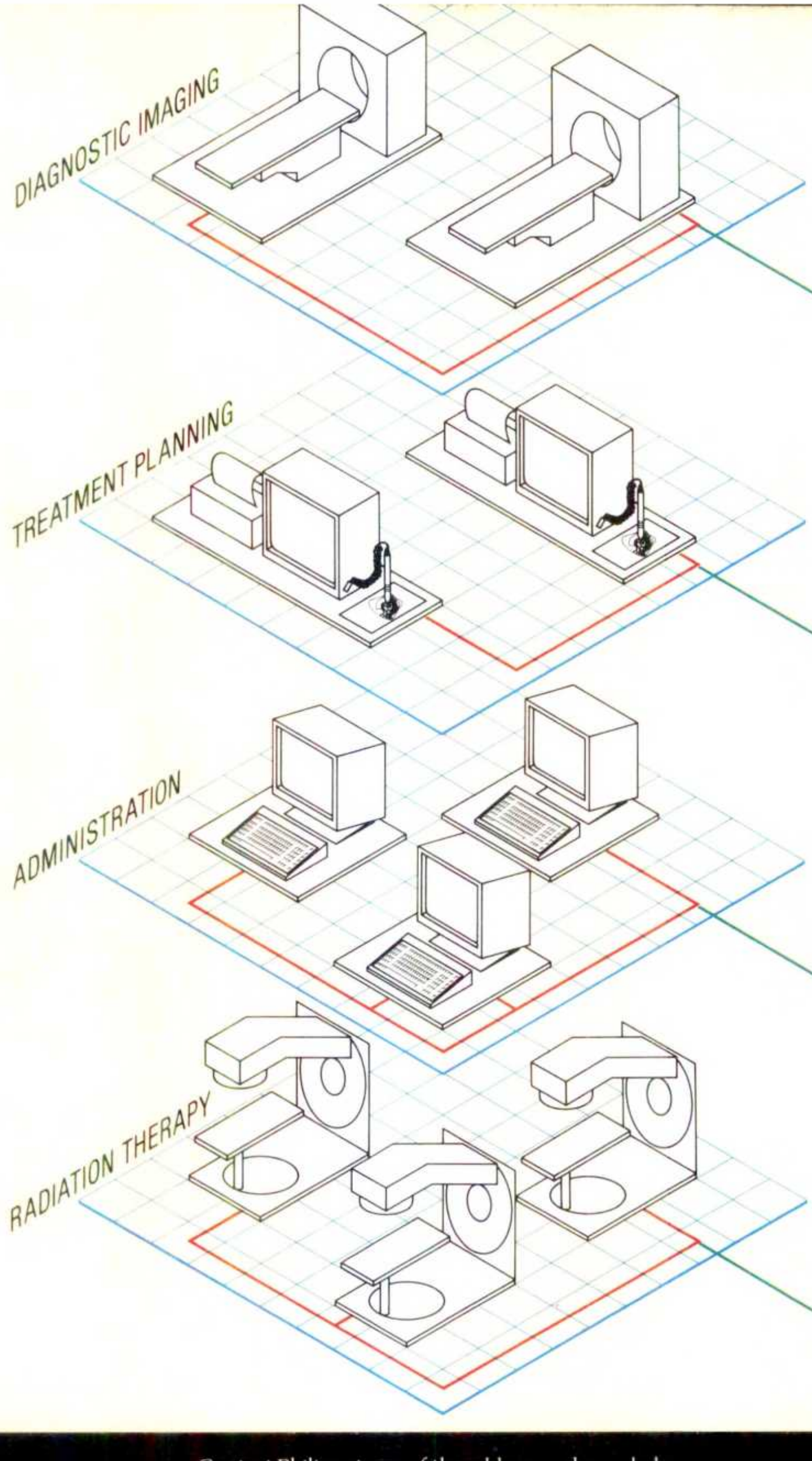

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1987, *The British Journal of Radiology*, *60*, 637–644

VOLUME 60 NUMBER 715 JULY 1987

The British Journal of Radiology

# Dysfunction of the pharyngo-oesophageal segment in patients with normal opening of the upper oesophageal sphincter: a cineradiographic study

By Olle Ekberg, M.D

Department of Diagnostic Radiology, Malmo General Hospital, S-214 01 Malmo, Sweden

(*Received August 1986*)

## Abstract

Abnormal opening of the upper oesophageal sphincter, *i.e.* abnormal relaxation of the cricopharyngeal muscle, is common in dysphagic patients. It is often present together with other motor abnormalities in the pharyngo-oesophageal (PO) segment, such as defective tonicity, relaxation and peristalsis. However, such PO motor dysfunction was demonstrated in 22 dysphagic patients who had *normal* relaxation of the cricopharyngeal muscle. Ten had defective peristalsis in the segment cranial to the cricopharyngeus In eight of these, barium contrast medium was retained at the end of the bolus passage. In one patient the cricopharyngeal muscle contracted too early ahead of the peristalsis. In four patients peristalsis and tonus were defective within the cervical oesophagus. In 145 non-dysphagic volunteers, with normal relaxation of the cricopharyngeal muscle, there was no such motor dysfunction in the PO segment. Our observations indicate that motor function of the PO segment is normally synchronous and symmetrical Motor dysfunction within the PO segment is rare but is detectable with a cineradiographic technique. In the absence of other morphological and functional abnormalities within the pharynx proper, it is probable that these motor dysfunctions in a dysphagic patient may have importance for the development of symptoms.

Dysfunction of the pharyngo-oesophageal (PO) segment in terms of cricopharyngeal inco-ordination is well known (Seaman, 1969, Ellis, 1971; Hellemans & Vantrappen, 1974; Ekberg & Nylander, 1982a, b; Curtis et al, 1984; Goyal, 1984; Ekberg & Wahlgren, 1985). It is generally believed to cause dysphagia. The radiological appearance is often conspicuous. Patients with such a cricopharyngeal impression may also have other motor dysfunctions in the PO segment above and below the cricopharyngeal muscle, for example, weak or absent peristalsis, defective tonicity between swallows and abnormal timing. Such concomitant motor dysfunctions are present in different combinations and might be as important symptomatically as cricopharyngeus inco-ordination. However, most patients with cricopharyngeal dysfunction have otherwise normal motor function of the PO segment. The aim of the present study was to describe the opposite circumstances, dysfunction of the PO segment in patients with normal relaxation of the cricopharyngeal muscle, which is a much rarer entity.

## Patients and Methods

A total of 22 patients were included in this retrospective study. They were collected out of a series of 950 dysphagic patients, examined during an 8-year period, who had been examined cineradiographically. There were 11 men and 11 women aged between 27 and 87 years (mean 61 years). They had been examined in an upright position in antero-posterior (AP) and lateral projections using 16 mm or 35 mm cine film at a frame rate of 50 per second. At least two medium-large swallows of barium contrast medium in each projection were studied. Several dry swallows were also documented.

The cineradiographs obtained were reviewed for the presence of functional abnormalities of the pharynx proper, *i.e.* epiglottic mobility, closure of the rima glottidis and laryngeal vestibule, as well as peristalsis in the pharyngeal constrictor musculature. Functional abnormalities in the PO segment were described in terms of tonicity between swallows, distensibility at the initiation of swallowing and peristalsis for propulsion of the tail of the barium bolus inferiorly

Only patients who had normal relaxation of the cricopharyngeal muscle were included, that is, the cricopharyngeal muscle was not seen as a posterior impression in the PO segment when the cervical oesophagus was distended by barium bolus. Patients who had undergone cricopharyngeal myotomy were also excluded. Patients who fulfilled these criteria but had abnormal motor function of the PO segment were included.

Two patients had had radiotherapy to the neck followed by surgery because of thyroid carcinoma. One of these patients was treated with a stent because of tracheal stenosis. Four patients had myotonic dystrophy. The other patients had no concomitant disease or treatment pertinent to the pharynx or cervical oesophagus.

The PO segment was defined as the transition between the pharynx proper and the cervical oesophagus, having a length of about 5 cm. It was assessed as having three subsegments: a cranial subsegment above the cricopharyngeal muscle which normally was collapsed between swallows, an intermediate

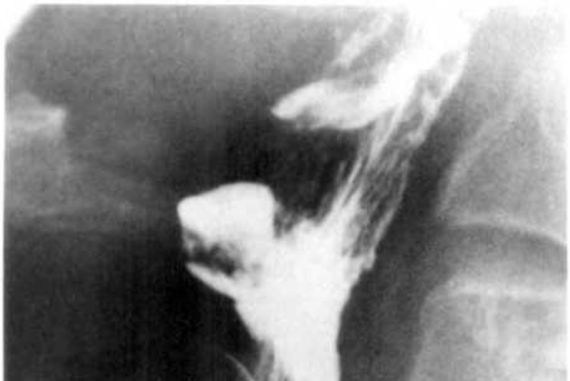

FIG. 1.

Lateral pharyngogram during barium swallow in a patient with a moderate posterior impression overlying the cricopharyngeus. The PO segment is distended and the three subsegments are indicated, namely: superior (s), middle (m) and inferior (i). The fifth vertebral body of the cervical spine is also indicated.

segment at the level of the transverse portion of the cricopharyngeus and an inferior subsegment below the cricopharyngeal muscle (Fig. 1) (Goyal, 1984). This inferior subsegment was longer with no sharp demarcation from the cervical oesophagus.

One hundred and forty-five non-dysphagic volunteers were also included as a control group*. They were cineradiographically examined in a similar way and had normal relaxation of the cricopharyngeus. Their cineradiographs were reviewed for the presence of motor dysfunctions of the PO segment other than defective relaxation of the cricopharyngeal muscle.

## RESULTS

Ten patients had abnormal peristalsis in the cranial segment. In two of these there was no peristalsis within the whole extent of the cranial subsegment. In these two patients there was even cessation of tonicity between swallows (Fig. 1). In eight of the 10 patients the defective peristalsis was confined to less than a segment 5 mm long immediately cephalad to the cricopharyngeus, from which contrast medium was not propelled inferiorly before contraction in the cricopharyngeal muscle occurred. Thereby, a small amount of barium contrast medium was retained above the cricopharyngeal muscle after the passage of the bolus (Figs 2–4). This was seen in both frontal and lateral projections. This retained contrast medium was expressed either inferiorly (Fig. 2) or superiorly (Fig. 4) a few seconds after the passage of the bolus. In patients where the retained barium was transported inferiorly, the cricopharyngeal muscle did open, allowing the contrast medium to flow inferiorly through a 1 mm slit.

In one patient the cricopharyngeal muscle contracted too early (Fig. 5). There was normal peristalsis and normal timing in the pharynx proper and also in the inferior pharyngeal constrictor. However, as peristalsis passed from the middle to the inferior pharyngeal constrictor, the cricopharyngeal muscle contracted vigorously, causing retention of contrast medium within the pharynx at the level of the inferior constrictor. This segment was even slightly ballooned, especially as the inferior pharyngeal constrictor showed an abnormally strong indentation and contracted vigorously. Retained contrast medium was then slowly pushed inferiorly beyond the cricopharyngeal muscle impression.

Defective tonicity and peristalsis of the inferior subsegment was seen in four patients. In these the cervical oesophagus was open between swallows and the peristalsis did not pass through the segment. However, no retention of barium occurred as the patients were examined in the upright position and the bolus flowed inferiorly due to gravity. One of these patients had been treated with radiotherapy and surgery for thyroid carcinoma. Another patient had mucosal moniliasis of the cervical oesophagus.

Four patients had defective tonicity of the inferior pharyngeal constrictor, cricopharyngeus and cervical oesophagus. They all had myotonic dystrophy.

Concomitant abnormalities in the pharynx proper were seen in 10 of the 22 patients. In seven patients there was epiglottic dysmobility, while eight had defective closure of the laryngeal vestibule. One patient had paresis of the superior and middle pharyngeal

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*These control patients were non-dysphagial volunteers who were being investigated for other conditions. The pharyngeal examinations were approved by the Ethical Committee of the University of Lund and Malmö General Hospital on December 13, 1979 (ref. No. 144/79).

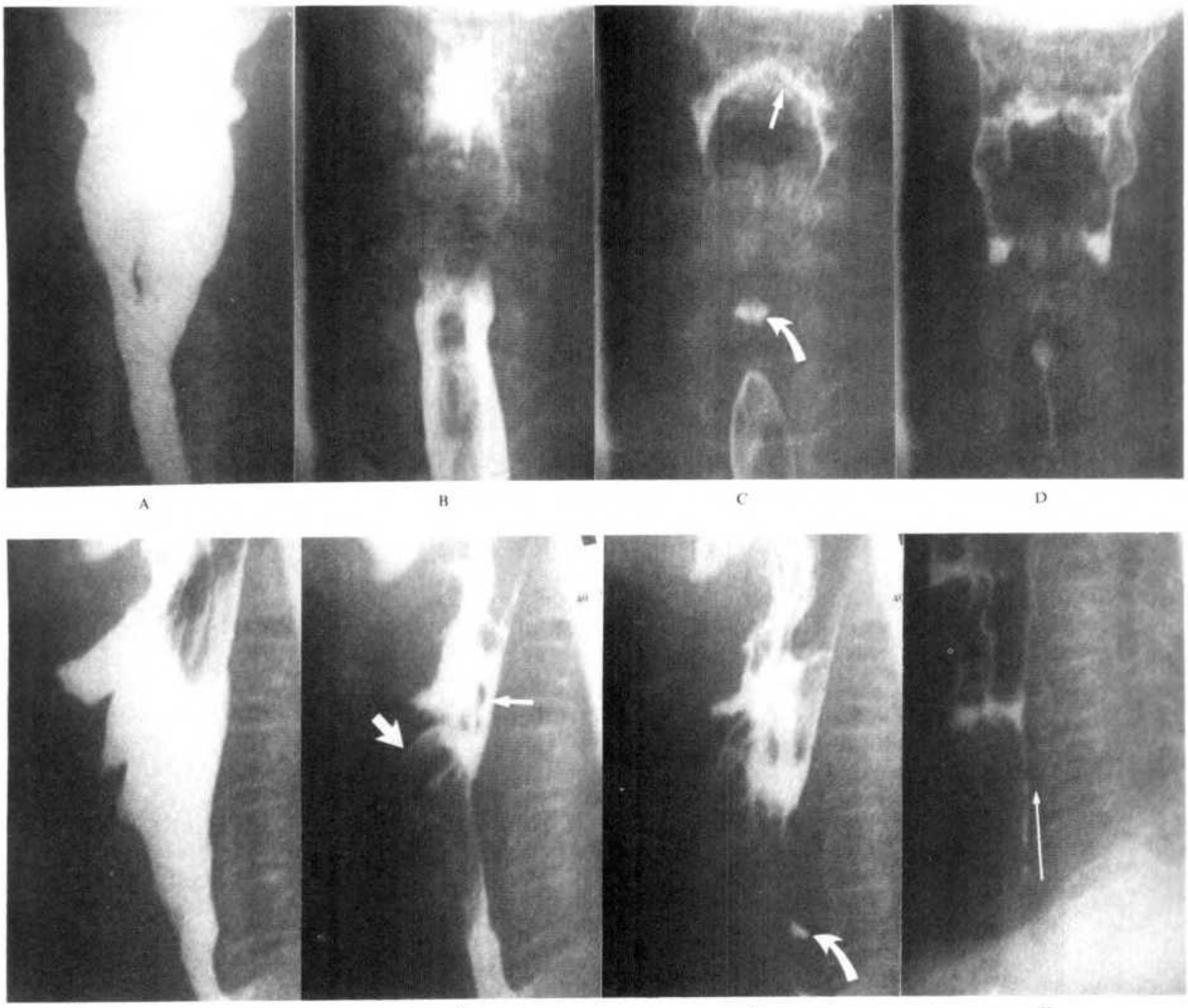

FIG. 2.

(A–H) A 75-year-old man with dysphagia; lateral projection. There is impaired mobility of the epiglottis (small arrow); its downward movement is only to the transverse plane. Contrast medium penetrates into the laryngeal vestibule (large arrow), indicating defective closure. Peristalsis is absent in the pharyngeal constrictors. A small amount of contrast medium is retained (bent arrow) above the cricopharyngeal sphincter. The cricopharyngeal sphincter relaxes normally. Between swallows, after the passage of the barium bolus, the barium retained above the cricopharyngeal muscle is emptied in a cranial direction (long arrow).

constrictors. Two patients had thin webs in the PO segment.

None of the 145 non-dysphagic volunteers had any motor dysfunction of the PO segment.

## DISCUSSION

The transition between the pharynx proper and cervical oesophagus (the PO segment) has a complex anatomy and intricate efferent innervation (Kirschner, 1958; Lund & Ardran, 1964; Lund, 1965; Doty, 1968; Murakami et al, 1972; Miller, 1982). It is frequently the location of dysfunctions as well as morphological abnormalities in patients with swallowing complaints (Seaman, 1969; Ekberg & Nylander, 1982b, 1983; Ekberg et al, 1985). However, because of its location between the pharynx and the oesophagus it is often overlooked at radiological examinations. It is open for only a fraction of a second during the passage of the barium bolus and is therefore difficult to examine with conventional single-radiograph techniques. Video and cineradiographic techniques are necessary for proper assessment.

Anatomically the PO segment, which is made up of

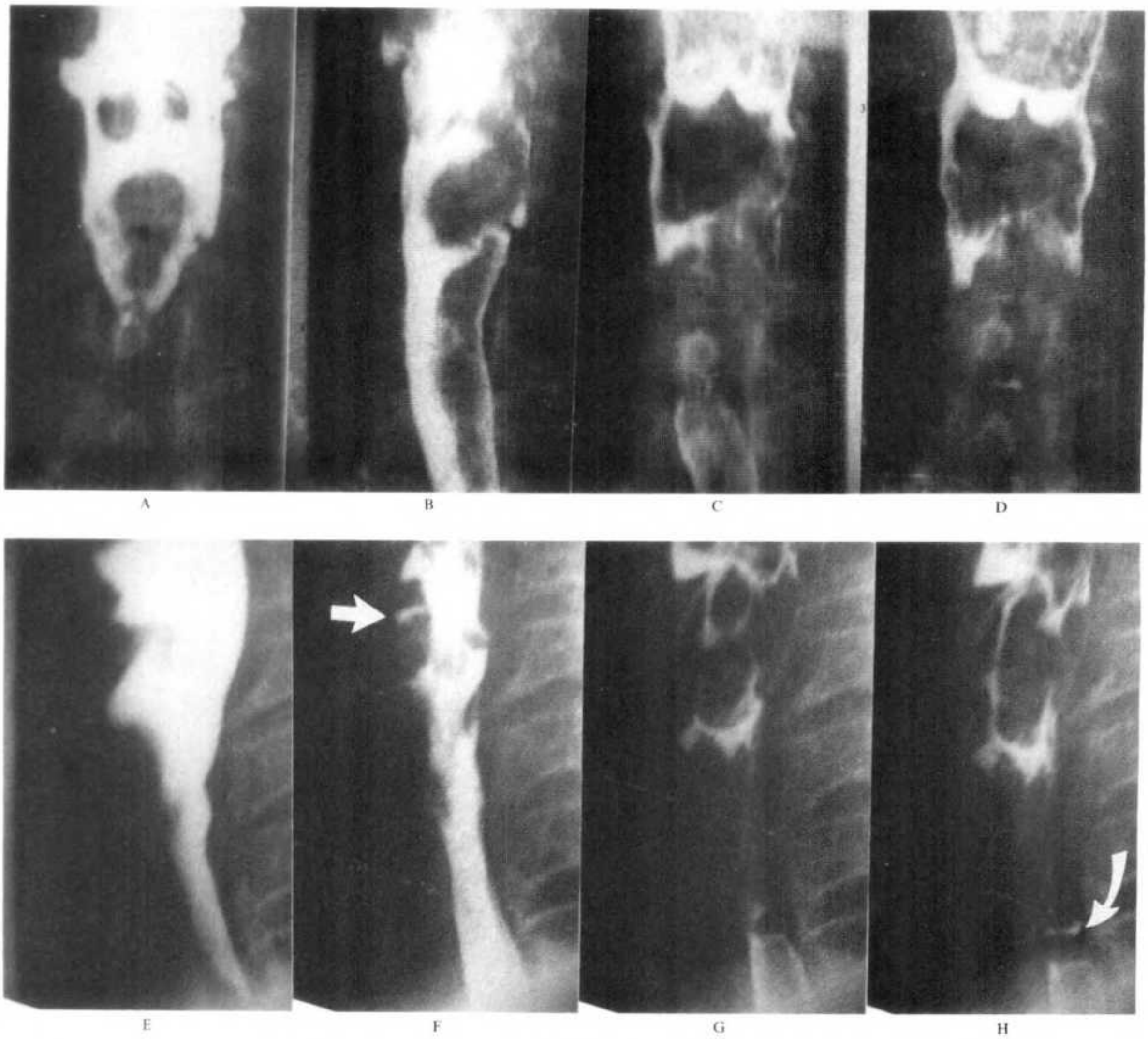

FIG. 3.

(A–H) A 79-year-old man with dysphagia; lateral projection. Contrast medium penetrates the laryngeal vestibule (large arrow). There is retention of barium (bent arrow) cranial to the cricopharyngeal muscle. The cricopharyngeal muscle relaxes normally. The retention is due to defective peristalsis within the cranial subsegment of the PO segment. There is defective peristalsis and tonicity within the inferior subsegment of the PO segment.

striated musculature, can be divided into a superior, a middle and an inferior portion (Goyal, 1984). The superior portion is located at the level of the thyropharyngeal muscle. Fibres from the stylopharyngeal, palatopharyngeal and salpingopharyngeus muscles as well as the oblique portions of the cricopharyngeal muscle are also part of the superior portion. At the transition between the superior and middle portion of the PO segment there is a triangular area between the oblique and transverse portions of the cricopharyngeal muscle which regularly lacks muscular support. This has been called the Laimer's triangle. The middle portion consists of the transverse portion of the cricopharyngeal muscle which is attached to each side of the cricoid lamina. This portion of the cricopharyngeus has no posterior midline raphe. The inferior portion of the PO segment is made up of the circular musculature of the cervical oesophagus. There is also a longitudinal portion of the cricopharyngeal muscle which is attached to the lateral aspect of the cricoid lamina. The attachment of the longitudinal musculature of the oesophagus to the cricoid cartilage is in the

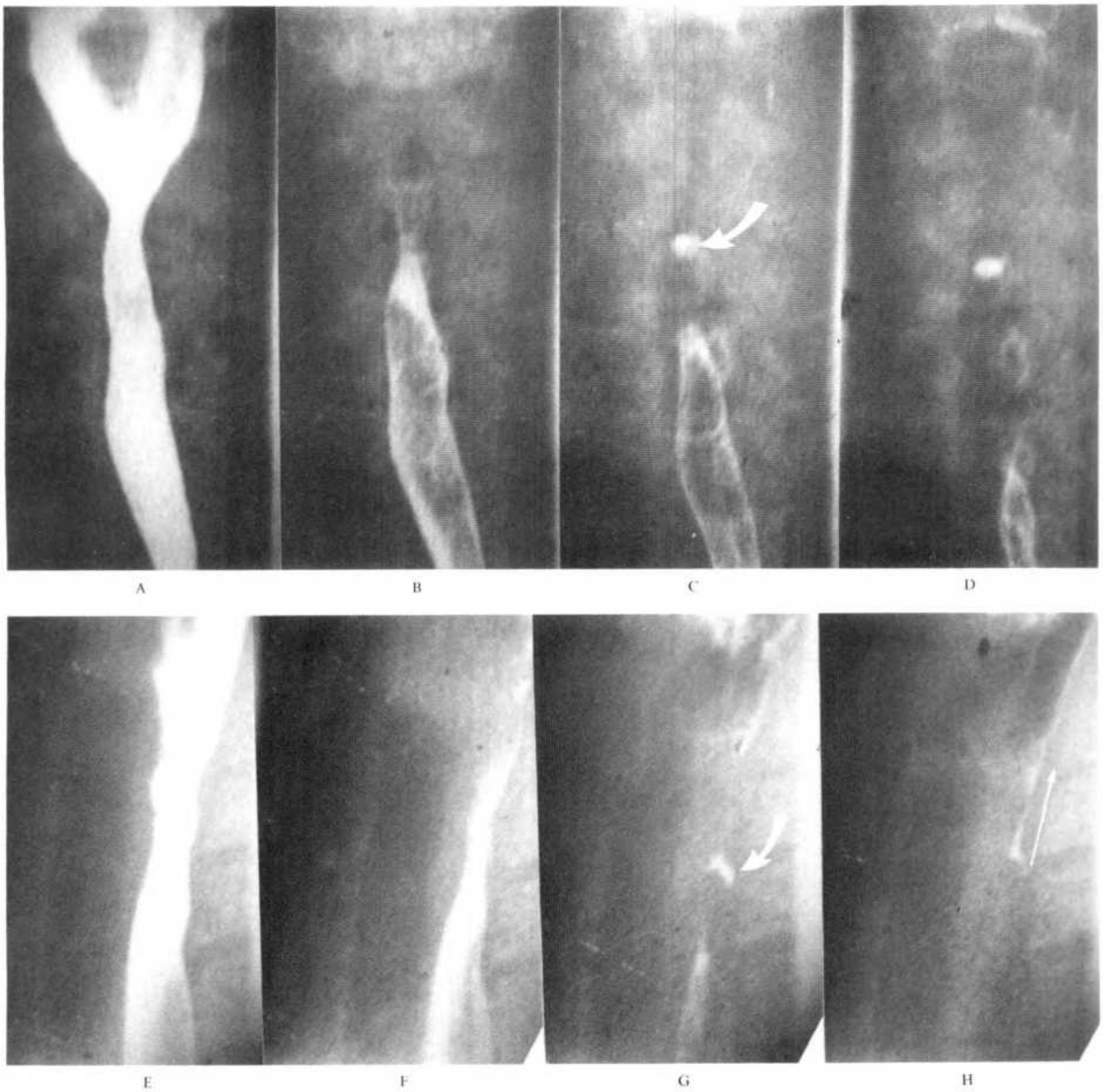

FIG. 4.

(A–H) A 60-year-old woman with dysphagia. There is retention of barium (bent arrow) above the cricopharyngeus. The cricopharyngeus relaxes normally. After swallowing the retained barium is emptied in a cranial direction (long arrow).

anterior midline. There is no longitudinal muscular support posteriorly within this subsegment.

The motor-neural control of the PO segment is still not fully mapped out and is partly contradictory. The afferent sensory innervation from the pharynx and the PO segment is represented in the tractus and nucleus solitarius in the medulla oblongata. Efferent motor function to the pharynx is mediated via the ninth and 10th cranial nerves, whose motor neurons are in the nucleus ambiguous. Co-ordination of control of swallowing is located in the middle and ventral aspect of the medulla and forms the swallowing centre. Between swallows, the PO segment is maintained in tonic contraction. This stable tonus is evidenced manometrically as sustained positive pressure.

From cineradiographic observations, the PO segment has three different principal functions. The first is the sphincteric function, which is well documented by

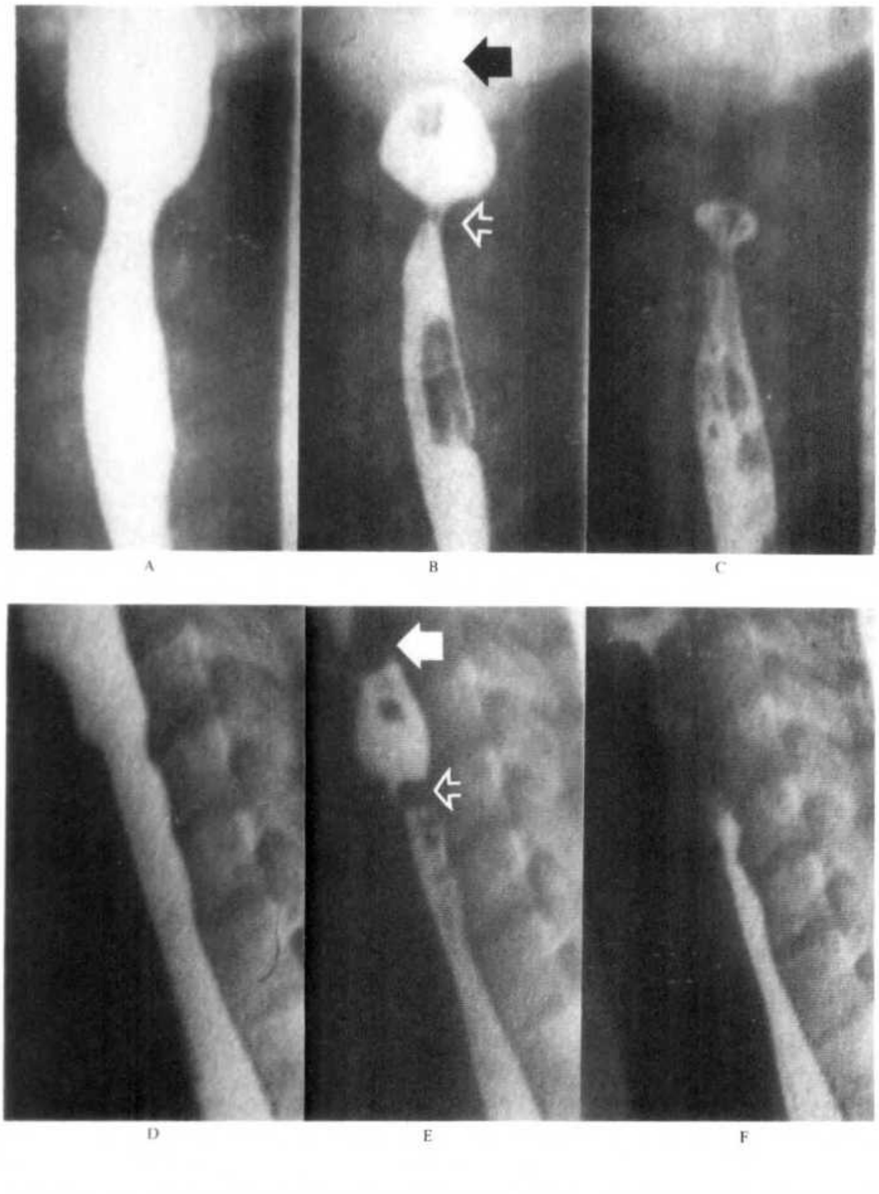

Fig. 5.

(A–F) A 21-year-old woman. There is a conspicuous premature contraction of the cricopharyngeal muscle (open arrow). There was transient retention of contrast medium cranial to the cricopharyngeal impression. There is vigorous contraction in the middle and inferior pharyngeal constrictor (solid arrow).

manometric and radiographic investigations. The second is relaxation at the initiation of pharyngeal swallow. The third is participation in the co-ordinated peristalsis of the pharynx above and oesophagus below. The peristalsis reflects co-ordination established in the brain stem.

Defective relaxation of the cricopharyngeal muscle is a conspicuous radiological finding in 25% of dysphagic patients (Ekberg & Wahlgren, 1985). In these, the cricopharyngeal muscle is seen as a posterior impression in the PO segment during the passage of the bolus. The posterior impression may be visible during different periods of bolus transit. However, it is always possible to see it at the early stage. It may then either be effaced or be sustained as an impression during the whole passage of the bolus. Moreover, there is regularly retention of barium contrast medium above the cricopharyngeal muscle in these patients. This reflects either an early contraction of the muscle or weakness of the inferior pharyngeal constrictor whereby part of the bolus is retained cranially. This has been called a pseudodiverticulum (Ekberg & Nylander, 1982b). Such a pseudodiverticulum is not correlated with the development of a Zenker's diverticulum, although these protrude at the same location in the Laimer's triangle (Ekberg & Wahlgren, 1985). The pseudodiverticulum is therefore not an abnormality *per se* but an important indicator of cricopharyngeal inco-ordination. Such a pseudodiverticulum has not previously been demonstrated radiologically in a patient with normal relaxation of the cricopharyngeal muscle. In a patient with normal relaxation of the cricopharyngeus, the pseudodiverticulum may reflect absence of peristalsis within the inferior few millimetres of the superior portion of the PO segment. Barium is thereby retained when the cricopharyngeal muscle contracts as part of its peristaltic activity. However, a few seconds later the contrast medium was regularly expressed in either an inferior or a superior direction, indicating that there is muscle within this segment. It can be explained by an assumption that the tonicity between swallows within this segment is normal while peristalsis is erratically controlled. The timing of contraction of the cricopharyngeal muscle seemed to be correct, even if difficult to assess. Peristalsis was missing in the particular portion superior to the cricopharyngeal muscle.

In only one patient was there a conspicuous premature contraction of the cricopharyngeal muscle. In that patient there was also a compensatory hyperactivity of the middle and inferior pharyngeal constrictors seen on the AP and as a prominent posterior impression on the lateral projection. Abnormal timing of peristalsis in the PO segment is a frequent finding during manometry. It is therefore interesting that premature contraction of the cricopharyngeal muscle is infrequently seen radiologically. This might be due to technical factors during manometry because the manometric device does regularly move a considerable distance through the PO segment during swallowing (Isberg et al, 1985). This is partly compensated for by using transducers with multiple holes. However, erratic timing of peristalsis in the PO segment is more accurately assessed during cineradiography, as the whole segment can be visualised simultaneously.

Impaired tonus between swallows and weak or absent peristalsis within the inferior subsegment and cervical oesophagus were seen as an isolated phenomenon in four of our patients who had normal motor function of the intermediate and cranial subsegments. In these patients the barium fell inferiorly due to gravity and between swallows the lumen was only partly collapsed. The width of the lumen varied slightly between swallows, probably due to respiration. One of the patients had oesophageal moniliasis, which has been shown to affect peristalsis within the thoracic oesophagus and was probably the cause of the motor dysfunction in this patient. However, in none of the patients was the motor function of the thoracic oesophagus examined In the other patients there were no morphological abnormalities which could be responsible for the lack of peristalsis.

More serious motor dysfunction included absent tonicity and peristalsis and was revealed in four patients with myotonic dystrophy Involvement of striated musculature within the pharynx and cervical oesophagus is common in this disease.

Two patients had had surgery and radiotherapy to the neck for thyroid carcinoma. One of these showed the most serious dysfunction, with defective peristalsis and tonicity in the whole PO segment. The other patient had a circumscribed defective tonicity and peristalsis within the inferior portion. This last patient also had a stent in the trachea. It is obvious that radiotherapy can interfere with the co-ordinated motor function of the PO segment. This has already been shown in patients with chalasia of the cricopharyngeal muscle as well as after myotomy for Zenker's diverticula (Logemann & Bytell, 1979; Goyal, 1984; Ekberg et al, 1985; Ekberg & Lindgren, 1987).

The observations of various motor dysfunctions of the PO segment in patients with normal relaxation of the cricopharyngeal muscle illustrate the complexity of co-ordinated motor function. Weak or absent function was present in different combinations. In nine of 22 patients there were functional abnormalities also in the pharynx proper in terms of defective closure of the laryngeal vestibule, dysmotility of the epiglottis and constrictor paresis. In these patients the relationships between symptoms and PO dysfunction is not obvious. However, in 13 other patients the observed dysfunction was the only abnormality registered. In these it is probable that the observed dysfunction is related to the patient's symptoms. This is made even more probable when compared with the 145 non-dysphagic volunteers, none of whom had any such motor abnormality of the PO segment.

The underlying pathogenetic mechanism for the development of these motor dysfunctions was not revealed except in a few patients, for example, moniliasis of the cervical oesophagus Surgery and radiotherapy to the neck might have pathogenetic importance in two patients. In the other patients it could not be determined whether the dysfunction was local, neuronal or muscular. It might reflect pathology within the efferent nerves or within the central representation of swallowing in the brain stem or at an even higher level.

The fact that 145 non-dysphagic volunteers had symmetrical and synchronous motor function of the PO segment during swallowing indicates the stability of swallowing performance in normal circumstances. The motor dysfunctions described within the PO segment in dysphagic patients seem to be rare. Some of these dysfunctions might be difficult to observe, *e.g.* defective tonicity and peristalsis of the cervical oesophagus. Others are conspicuous, such as the retention of barium above an early-contracting cricopharyngeal muscle

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1987, *The British Journal of Radiology*, *60*, 645–648 JULY 1987

# The importance of appropriate frequency selection in sonographic gallstone detection

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(*Received August 1986*)

ABSTRACT

A prospective study was performed on 161 patients referred for gallbladder ultrasound to determine whether routine use of a 5 MHz probe in addition to a standard 3.5 MHz probe provided useful additional information Seventy-two patients were found to have gallstones In 26.4% of these patients (19 cases) a confident diagnosis of gallstones was possible only when the 5 MHz probe was used. These results confirm theoretical assertions on the value of high-frequency probes in the evaluation of superficially located organs such as the gallbladder Our findings lend support to their routine use in cholecystosonography.

Ultrasound is accurate in the diagnosis of gallstones (Crade et al, 1978; Cooperberg & Burhenne, 1980; Laing, 1984) Several authors have mentioned the importance of using high-frequency, short- or medium-focus probes, to improve the accuracy of gallbladder examination (Cooperberg, 1982; Laing, 1984) and *in-vitro* studies support these suggestions (Carroll, 1978; Filley et al, 1979). To the best of our knowledge, no clinical trial has been performed to confirm these observations. This study was undertaken to determine whether routine use of a short-focus 5 MHz probe, in addition to a standard, medium-focus 3.5 MHz probe, provided useful additional information in gallstone detection.

## PATIENTS AND METHODS

Over a 3-month period, 161 patients were referred for ultrasound examination of the gallbladder All patients were examined in a fasting state using a conventional real-time sector scanner. Both a 3.5 MHz probe focused at 8.0 cm and a 5.0 MHz probe focused at 3.5 cm were used in all patients. The examination technique included the supine and oblique decubitus positions in all patients, with lateral and erect positioning as necessary. Appropriate alterations in beam intensity and gain settings were performed for each patient (Taylor et al, 1979). At least two authors were in attendance at each examination.

The sonographic findings were classified into three categories for each probe:

(1) normal gallbladders,
(2) gallbladders containing unequivocal gallstones; and
(3) gallbladders demonstrating other abnormalities.

Included in Category 2 are contracted gallbladders containing calculi demonstrating the "WES" or "double-arc-shadow" signs, as described by MacDonald et al (1981) and Raptopoulos et al (1982) respectively

Further investigations were not recommended in patients who definitely had gallstones, but were performed at the discretion of the referring clinician All patients in Category 3 and some in Category 1 had further investigations, including oral cholecystography.

The results of the ultrasound examination were compared with the findings of other investigations, including operative findings when surgery was performed.

## RESULTS

Of 161 patients studied, ultrasound was the initial method of investigation in 153 cases. The gallbladder was visualised in all cases, the mean depth of the anterior gallbladder wall being 3.6 cm ± 1.1 cm.

In 73 patients (45.3%) the gallbladder appeared normal using both probes. An unequivocal diagnosis of gallstones was made in 72 patients (44.7%) (Tables I and II). Non-calculous gallbladder disease was diagnosed in 16 patients (10%). The findings in this latter group will form part of a separate report.

Of patients with gallstones, in 68% of cases (49 out of 72) a positive diagnosis was possible using either probe. However, in 26.4% of cases (19 out of 72), gallstones could be diagnosed with certainty only with the 5 MHz probe. In seven of these 19 patients, the 3.5 MHz probe demonstrated an "echo-shadow"

TABLE I

DEMONSTRATION OF GALLBLADDER PATHOLOGY IN CATEGORY 1 AND 2 PATIENTS

| Probe used in examination | Number of patients | |
|---|---|---|
| | Category 1 (normal) | Category 2 (Unequivocal gallstones) |
| 3.5 MHz probe | 73 | 53* |
| 5.0 MHz probe | 73 | 68* |
| Both probes | 73 | 72 |

*In 49 cases gallstones were demonstrated using both the 3.5 MHz and the 5 0 MHz probe.

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*Author for reprint requests.

TABLE II

DIAGNOSIS OF GALLSTONES IN CATEGORY 2 PATIENTS

| Probe with which diagnosis obtained | Number of patients |
|---|---|
| Both probes | 49 |
| 5.0 MHz probe only | 19 |
| 3.5 MHz probe only | 4 |
| Total | 72 |

complex in the region of the gallbladder fossa, an appearance suggestive, but not diagnostic, of gallstones in a contracted gallbladder (Fig. 1A). In all seven, however, use of the 5.0 MHz probe allowed visualisation of the anterior wall of the gallbladder and its residual lumen, in addition to the "echo-shadow" complex. This appearance, the so-called "WES" sign, permitted a confident diagnosis of gallstones (Fig. 1B). In the remaining 12 patients in this group, small, non-shadowing opacities were shown in the gallbladder with the 3.5 MHz probe (Fig. 2A). In all 12, use of the 5.0 MHz probe demonstrated associated posterior acoustic shadowing (Fig. 2B).

In four patients whose gallbladders were deeply positioned (mean depth of anterior wall 7.1 ± 1.1 cm versus 3.6 ± 1.1 cm for the group as a whole) shadowing opacities diagnostic of gallstones were shown with the 3.5 MHz but not the 5.0 MHz probe.

To date, 45 of the 72 patients with a sonographic diagnosis of gallstones have proceeded to surgery with operative confirmation in every case. Included within this group are 16 of the 19 patients in whom stones were diagnosed with the 5.0 MHz but not the 3.5 MHz probe.

Thirty-eight of the 73 patients whose gallbladders were sonographically normal underwent oral cholecystography. In no case has a false negative sonographic diagnosis been revealed using this method.

## DISCUSSION

A confident diagnosis of cholelithiasis can be made only in patients whose gallbladders contain echogenic structures which are associated with posterior acoustic shadowing. Unless this strict diagnostic criterion is met in full, errors in diagnosis of gallstones are likely (Crade et al, 1978; Simeone et al, 1980; Cooperberg, 1982).

Calculi attenuate the ultrasound beam to produce posterior acoustic shadowing by two processes: specular echo production and sound absorption. Between 20% and 30% of the energy of the incident ultrasound beam is reflected at the bile–stone interface by specular echo production. Further attenuation of the incident beam is by sound absorption in the stone. It is this, rather than reflection, which is largely responsible for posterior acoustic shadow formation (Sommer & Taylor, 1980).

*In-vitro* studies have analysed the various factors which govern shadow formation. Stone size is of major importance. Using 2.25 MHz, 3.5 MHz and 5.0 MHz probes, Carroll (1978) was unable to demonstrate shadowing deep to stones of less than 3.0 mm in diameter. A similar study showed shadowing with stones as small as 2.0 mm when a 5.0 MHz probe was used (Grossmann, 1978). Both authors concluded that shadowing from smaller stones was more readily demonstrated when high-frequency (5.0 MHz) probes were used.

Apart from size, do any other stone parameters influence shadow formation? Several authors were unable to relate the incidence of shadowing to surface characteristics, shape, chemical composition or structure of calculi (Carroll, 1978; Filly et al, 1979; Good et al, 1979). These observations are at variance with those of Purdom et al (1980) who found

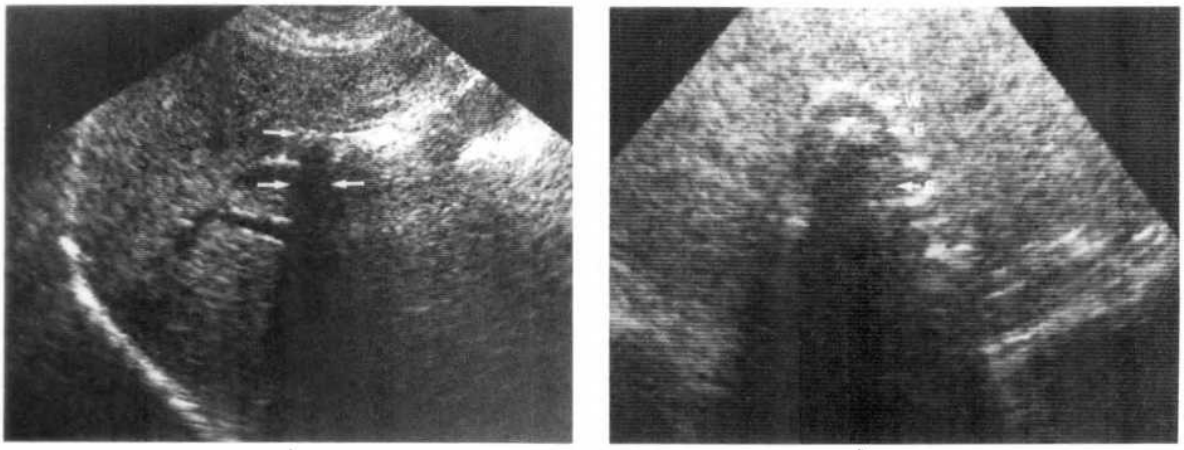
A B

FIG. 1.

(A) "Echo-shadow" complex arising from the gallbladder fossa (arrows) (3.5 MHz probe). (B) With the 5 MHz probe the "WES" sign (arrows) is demonstrated allowing confident diagnosis of gallstones.

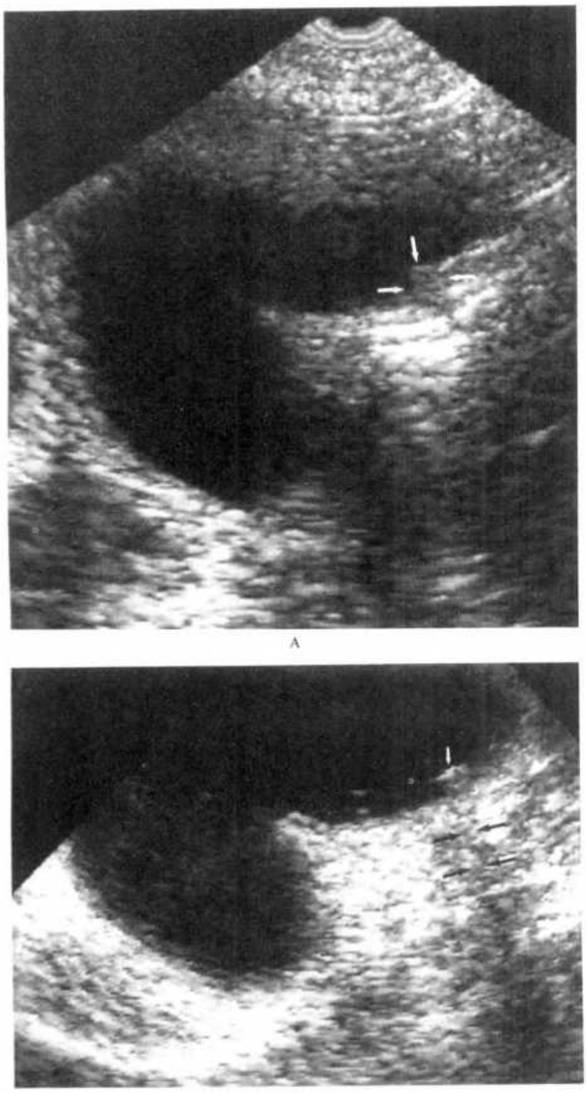

FIG. 2.

(A) Small, non-shadowing opacities (arrows) within the gallbladder seen with the 3.5 MHz probe (B) With the 5 MHz probe, posterior acoustic shadowing is evident (arrows). This indicates the presence of gallstones (operative proof).

differences in beam attenuation between stones of similar size but different chemical composition and structure. These differences showed marked frequency dependence, being greatest at higher frequencies.

Ultrasound beam focusing patterns are an important but frequently neglected factor in acoustic shadow production. Their importance is well illustrated by the work of Jaffe and Taylor (1979) and Filly et al (1979). For shadow production a stone must fulfil two related requirements: it should intercept the centre of the ultrasound beam; and its diameter must approach that of the ultrasound beam, or the ratio of its diameter to that of the beam must exceed a critical (as yet undefined) value. Both of these requirements are easily met when stones are large in relation to the beam width. With small stones, however, imaging the stone at or near the point of maximum beam focus (by using a transducer of suitable focal length) and alignment of the stone in the centre of the beam, both assume critical importance.

In this study, of 161 patients referred for sonographic examination of their gallbladders, 72 (44.7%) had gallstones demonstrated unequivocally. In 68% of cases (49 patients) the diagnosis of gallstones was made with confidence using either the 3.5 MHz or the 5.0 MHz probe. However, in the remaining 32% of cases (23 patients) appropriate probe selection was critical for accurate diagnosis. In 19 patients, the diagnostic criteria for gallstones were completely satisfied only when the short-focus 5.0 MHz probe was used. By contrast, in the remaining four patients whose gallbladders were deeply situated, a confident diagnosis of gallstones was possible only with the 3.5 MHz probe with its longer focus (8 cm).

In conclusion, this study confirms the importance of appropriate probe selection in the detection of gallstones. In the majority of patients, the superficially located gallbladder is best imaged using a short-focus, high-frequency probe. Of equal importance, however, in larger patients or in those in whom the gallbladder is more deeply located, optimal images are obtained with probes of lower frequency and longer focus. We therefore stress that reliance on a probe of single frequency in sonography of the gallbladder will provide less than adequate information in a significant number of patients.

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1987, *The British Journal of Radiology*, 60, 649–654 JULY 1987

# Scrotal ultrasonography: a clinical evaluation

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## ABSTRACT

Two hundred and thirty patients had scrotal ultrasonography over an 18-month period. We report the ultrasound findings, correlation with the clinical diagnosis and, where possible, with the pathological diagnosis The results show the value of scrotal ultrasonography in clinical practice Of particular interest is the ultrasonic examination of the clinically normal or impalpable testis and the correct ultrasound diagnosis of testicular tumour in five cases (2% of all cases, 28% of tumours detected) thought clinically to be benign. A brief review of abnormal appearances is included

The scrotal contents are well suited to ultrasound examination. This was first reported by Miskin and Bain (1974), who used static B-mode scanning. The advent of high-frequency, real-time ultrasound has improved both the ease of the examination and the image resolution. Some ultrasound probes have integral water-paths allowing good "stand-off" from the organ of interest and thereby producing an image free from near-field interference. The same effect can be produced by interposing sonoconductive gel (Kitecko) or a movable water-path such as a saline bag Some workers have devised compound scanners within a water bath into which the scrotum is lowered (Kimura et al, 1983). Generally it is satisfactory to use a direct-contact approach using only a thin layer of acoustic coupling gel.

## METHOD

Two hundred and thirty patients were referred for ultrasound examination over an 18-month period. Most were referred from the Department of Urology in this hospital where they had been examined by experienced surgeons. The putative diagnosis or diagnoses were entered on the request card and later compared with the ultrasound findings. When more than one clinical diagnosis was offered, the diagnoses were designated as primary or secondary, depending upon the level of clinical certainty indicated. If more than one abnormality was demonstrated by ultrasound, the findings were designated primary or secondary according to the importance of the disease process and its relevance to the presenting illness. Where possible, operative and pathological findings have also been correlated.

## TECHNIQUE

In this series a commercially available 7.5 MHz mechanical sector scanner was used. This particular model does not have an integral water-path. Occasionally an interposed water-path or gel equivalent was used but most scans were performed by direct-contact scanning The patients lay supine with the scrotum exposed. The thighs were fully adducted; a paper towel under the scrotum gave sufficient support. This is an embarrassing examination for the patient and should be performed with maximum privacy and consideration.

## NORMAL APPEARANCES

The testis is of homogeneous texture and medium-amplitude echogenicity. The mediastinum of the testis is often seen as an echogenic band in the long axis of the organ with fine strands radiating into the testicular tissue. The epididymis is of varying echogenicity; we found its head to be slightly more echogenic than the testis, while the main length of the epididymis is less echogenic than the adjacent testis, which agrees with the recent publication by Rifkin et al (1984). Other reports (*e.g* Leung et al, 1984) have suggested that the epididymis is relatively more echogenic throughout. Slight variations in relative testicular size are common but the echogenicity should be closely comparable.

## ABNORMAL APPEARANCES

### *Orchitis*

The characteristic appearance is of a diffusely hypoechoic testis. In the acute stage the testis is swollen; if atrophy occurs the testis will shrink, but it usually remains relatively hypoechoic (Bird & Rosenfield, 1984). Chronic low-grade inflammation may result in disorganisation of the scrotal contents, loss of testicular integrity and appearances mimicking tumour (Michell et al, 1985). Ischaemic, inflammatory and granulomatous orchitis (Klein et al, 1985) produce similar appearances. Associated skin thickening helps to distinguish inflammation from malignancy (Subramanyam et al, 1985).

### *Acute epididymitis*

This condition is readily diagnosed ultrasonically by the demonstration of a swollen, hypoechoic epididymis (Fig. 1). Such swelling may be gross, with resultant compression and deformity of the adjacent testis. Severe local inflammation (abscesses) are seen as areas of focal enlargement with markedly reduced internal echoes,

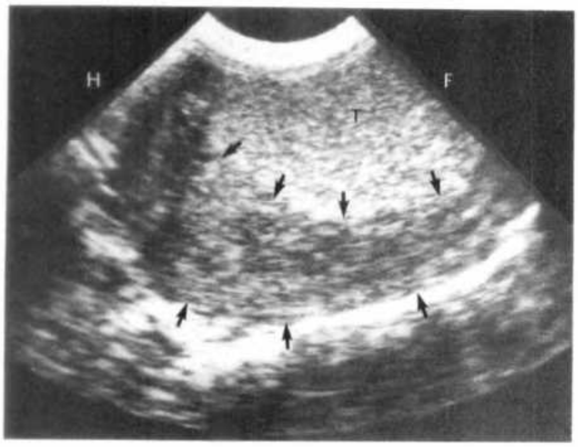

FIG. 1.
Acute epididymitis: the swollen hypoechoic epididymis is clearly shown (black arrows) in this longitudinal scan. The testis (T) is a little compressed but otherwise normal.

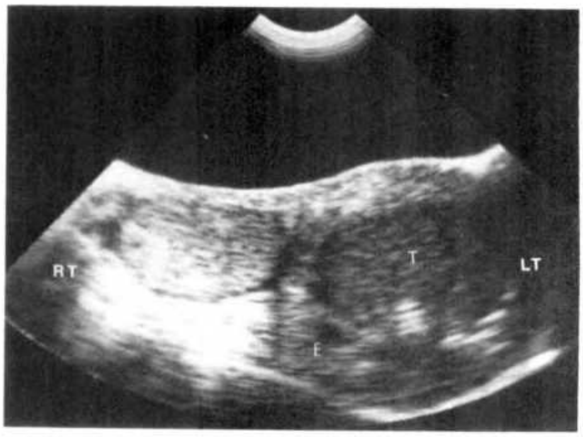

FIG. 2.
Epididymo-orchitis: the right hemiscrotum is normal. The left testis (T) and epididymis (E) are both swollen and hypoechoic.

occasionally echo-free and cystic. In this series they have been seen most frequently in the lower body and tail of the epididymis.

*Chronic epididymitis (peri-orchitis)*

The most characteristic finding is a thickened tunica albuginea and a thickened, somewhat irregular epididymis. Thickening of the fascial covering of the epididymis may occasionally be identified. Calcification is sometimes seen in the tunica albuginea and calculi may form in the tunica space (Linkowski et al, 1985). Adhesions may form between the tunica albuginea and vaginalis, loculating the scrotal fluid that is often in excess. Epididymal cysts or solid fibromas may be detected.

*Epididymo-orchitis*

Focal, echo-poor areas are seen in the testis adjacent to the most severe epididymal changes. In severe epididymo-orchitis the whole testis may be involved, the appearances then being a combination of acute epididymitis and acute orchitis, *i.e.* both structures swollen and of decreased echogenicity (Fig. 2). In our series true epididymo-orchitis was encountered much less frequently than had been suspected clinically.

*Focal epididymal lesions*

Cysts are readily identifiable within the epididymis. They may become sizeable, particularly in the epididymal head. Multiple cysts within the epididymal head may suggest spermatocoeles (Willscher et al, 1983). Solid lesions of the epididymis are often more difficult to define as their echogenicity tends to be comparable with that of the adjacent epididymis. Fibromas and sperm granulomas can be identified, but their appearances are non-specific. Differentiation of solid from cystic lesions can be performed with ease.

*Hydrocoeles*

Excess fluid in the scrotum can readily be visualised. The normal scrotum contains only a few ml of fluid. If a hydrocoele is large and tense there may be considerable compression of the testis with resultant deformity. Ultrasound is of great value in the examination of the testis rendered impalpable by a large surrounding hydrocoele (Fig. 3).

*Varicocoeles*

The normal testicular veins are often visualised with ultrasound, particularly in the upper scrotum. A varix appears as a collection of tubular structures with no "significant" internal echoes (*vide infra*). As such it poses no real problem in differentiation from epididymis and cord. With our 7.5 MHz transducer we have consistently been able to "visualise" the venous blood flow in varicocoeles. This results from a modified Doppler effect from the blood corpuscles within the veins and appears as unidirectional, tumbling echoes within the varix (Wolverson et al, 1983). Slight pressure upon the neck of the scrotum accentuates this phenomenon.

*Testicular trauma and torsion*

Trauma of the testis may, in its severest form, manifest as fracture which can be visualised as separation of testicular tissue. Intratesticular haemorrhage appears as diffuse areas of increased echogenicity often within a hypoechoic testis, reflecting infarction (Jeffrey et al, 1983). Changes may persist long after the patient is asymptomatic. Haematomas are often confined by the tunica albuginea compressing and deforming the underlying testicular tissue (Schaffer,

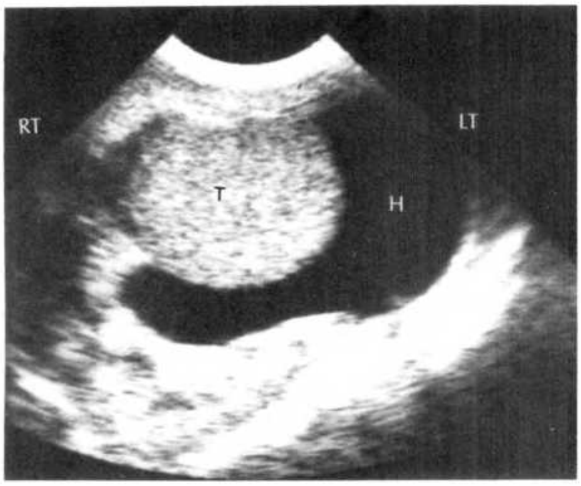

FIG. 3.

Transverse scan shows a large hydrocoele (H): the normal, but impalpable testis (T) is easily demonstrated.

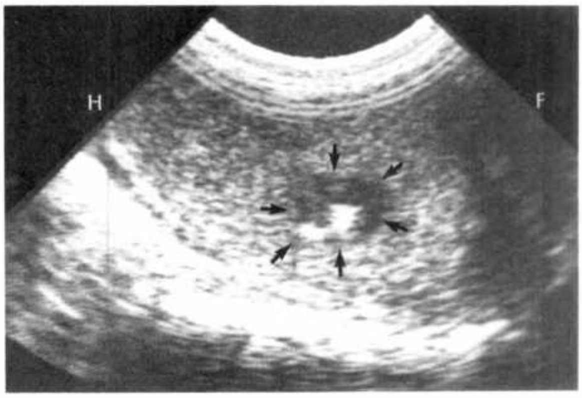

FIG. 4.

A longitudinal ultrasound scan shows a small central tumour (black arrows): the relatively hypoechoic germ-cell tumour contains dense hyper-reflective areas of fibrosis. This tumour was clinically undetectable.

1985). As with haematomas elsewhere in the body, these may become hypoechoic during resolution. Low-level echoes or septations within associated scrotal fluid should suggest haematocoeles (Cunningham, 1983; Jeffrey et al, 1983; Schaffer, 1985).

Torsion of the testis is not easy to diagnose confidently by real-time ultrasound and a negative or equivocal examination should not delay exploration when clinical suspicion is high. Doppler examinations have been found useful by some workers and radionuclide scanning can be very accurate (Stage et al, 1981).

The ultrasound appearances of torsion may be indistinguishable from orchitis or epididymo-orchitis with a testis that is diffusely or focally hypoechoic and often swollen. There may be accompanying swelling and reduced echogenicity of the epididymis, including echo-free "cystic" areas of haemorrhage. There is often an increase in fluid in the affected hemiscrotum. Clues to the diagnosis are abnormal positions of the testes, which may lie transversely or be inverted ("bell and clapper" position) and may be seen to be abnormally mobile. Orientation of the testis is achieved by visualisation of the epididymal head. A relevant clinical history in a patient of the appropriate age group is paramount. We have not found it possible to diagnose torsion of the appendix testis and indeed doubt if this is feasible.

### *Testicular tumour*

In general these are hypoechoic lesions within the testicular substance. If large enough they produce swelling of the affected side but, if small and central, cause no local deformity (Fig. 4). We have found tumours easy to differentiate from focal orchitis as they are generally better defined, have lower-amplitude internal echoes and, most significantly, show greater disorganisation of texture. Differentiation of tumour types has been described by many authors, but in general we have not attempted this exercise, for, having made the diagnosis of tumour, it seems of little practical value to estimate the histology. Seminomas are, in general, more homogeneous and more clearly defined than non-seminomatous tumours. We found a high incidence of highly echogenic focal areas within the embryonal-cell tumours, reflecting areas of dense fibrosis or calcification (Grantham et al, 1985). Cystic spaces within the tumour tissue are sometimes seen in teratoma and may fill the whole mass, giving the characteristic appearance of a cystic teratoma (Fig. 5). This must be distinguished from the rare condition of cystic dysplasia (Cho & Kosek, 1985). Primary lymphoma of the testis is usually seen in older patients and appears as a hypoechoic mass lesion with moderately well defined margins simulating seminoma. We have identified one case of Azzopardi scar where a metastasising teratoma of the testis had regressed, leaving no residual tumour within the testis (Azzopardi & Hoffbrand, 1965; Grantham et al, 1985). In this case para-aortic lymph-node biopsy confirmed teratoma of testicular origin. A rare case of recurrent rhabdomyosarcoma presented following orchidectomy with an irregular, complex mass of mixed echogenicity in the hemiscrotum of the removed testis. Metastases to the testis have been documented (Krone & Carroll, 1985), but we have not encountered any in this series. The ability of ultrasound to demonstrate occult or impalpable testicular tumours is well demonstrated (Glazer et al, 1982; Bockrath et al, 1983; Moudy & Makhija, 1983; Hendry et al, 1984; Stoll et al, 1986).

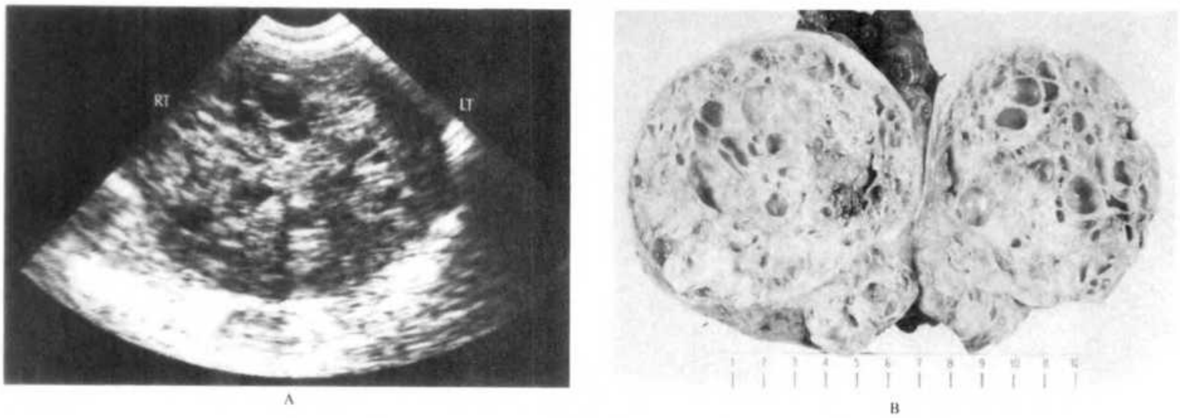

Fig. 5.

(a) The ultrasound appearances of a cystic teratoma in a transverse scan. (b) The cut specimen of the same tumour.

### Results

Ultrasound has proved accurate in terms of the final diagnosis reached, although in the cases of benign disease the "final" diagnosis is to a certain extent speculative, as the majority of the patients did not have biopsy or surgery. None of the patients diagnosed as having benign disease on ultrasonic criteria have developed stigmas of malignancy and most have resolved or responded to conservative treatment.

In the diagnosis of malignant disease, where pathological correlation was obtained, ultrasound achieved high accuracy, sensitivity and specificity and was clearly superior to clinical diagnosis. The comparative results are given in Table I. The two cases misdiagnosed by ultrasound were both false positive diagnoses of tumour in patients with indolent inflammation causing gross disorganisation of scrotal contents (Fig. 6). Both these cases had primary clinical diagnoses of benign disease, although the secondary clinical diagnosis was of tumour. Similar cases producing false positive diagnoses of tumour have been reported by Michell et al (1985).

There were 24 clinical false positive diagnoses of tumour, which to a certain extent must reflect appropriate clinical caution. Eight of these patients (33%) had hydrocoeles demonstrated by ultrasound and no other significant abnormality. Hydrocoele was, however, suspected clinically in only one of this group.

More significant were the five false negative clinical diagnoses of tumour. In all these cases, benign disease was the sole putative diagnosis. Malignancy was not considered as either primary or secondary clinical diagnosis. There were two further cases in which testicular malignancy was suspected clinically from the

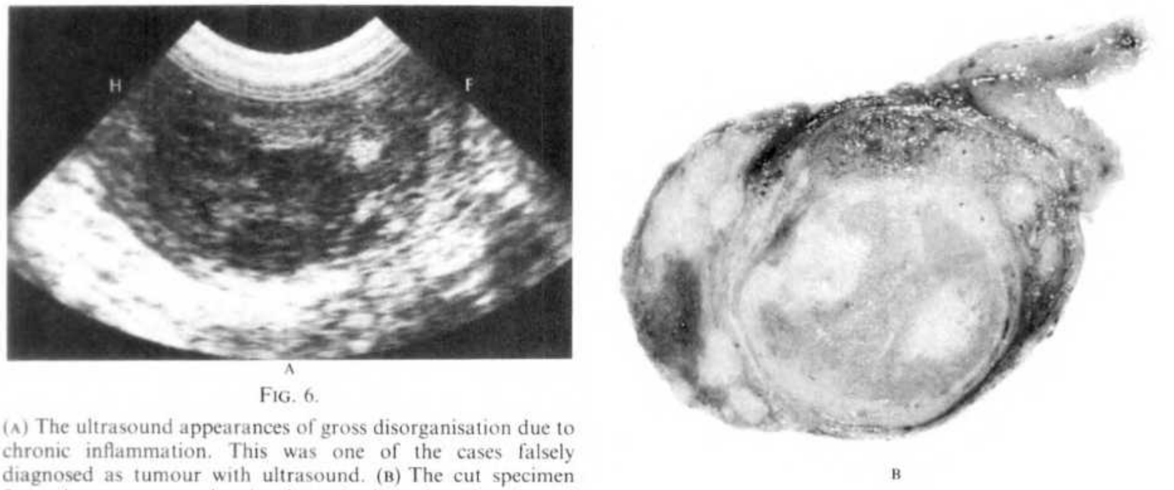

Fig. 6.

(a) The ultrasound appearances of gross disorganisation due to chronic inflammation. This was one of the cases falsely diagnosed as tumour with ultrasound. (b) The cut specimen from the same case, showing how the integrity of testis and surrounding structures has been lost.

TABLE I

RESULTS COMPARING CLINICAL AND ULTRASOUND DIAGNOSIS OF TUMOUR

| | Ultrasound | Clinical |
|---|---|---|
| True positive | 18 | 13 |
| False positive | 2 | 24 |
| True negative | 210 | 188 |
| False negative | 0 | 5 |
| Accuracy | 99% | 87% |
| Sensitivity | 100% | 72% |
| Specificity | 99% | 89% |

$$\text{Accuracy} = \frac{\text{True positive} + \text{True negative}}{\text{All}} \times 100\%$$

$$\text{Sensitivity} = \frac{\text{True positive}}{\text{True positive} + \text{False negative}} \times 100\%$$

$$\text{Specificity} = \frac{\text{True negative}}{\text{True negative} + \text{False positive}} \times 100\%$$

TABLE II

DIFFERENTIATION OF BENIGN AND MALIGNANT DISEASE

| Clinical diagnosis | Ultrasound diagnosis | Final diagnosis |
|---|---|---|
| Suspected tumour 37 | Tumour 13 | 13 Tumour |
| | | 0 Benign |
| | Benign 24 | 0 Tumour |
| | | 24 Benign |
| Clinically benign 193 | Tumour 7 | 5 Tumour |
| | | 2 Benign |
| | Benign 186 | 0 Tumour |
| | | 186 Benign |

site and type of distant metastases although the testes were thought clinically to be normal Ultrasound revealed a small, central, impalpable tumour in one case and an Azzopardi scar in the other (Azzopardi & Hoffbrand, 1965).

The differentiation of benign and malignant disease using ultrasound and on clinical examination is illustrated in Table II. Although these results compare the primary clinical diagnosis of tumour with the ultrasound results, no tumour was detected in any patient with a secondary clinical diagnosis of tumour. Where ultrasound confirmed a clinical diagnosis of benign disease (186 cases) it agreed with the type of benign disease clinically diagnosed in only 65% (120 cases).

In particular, clinically diagnosed epididymo-orchitis was confirmed by ultrasound in only 55% of cases (12 out of 22). Conversely, varicocoeles were convincingly demonstrated by ultrasound in 18 cases (8% of the series) Five cases were clinically suspected in the total series, but of these only two were confirmed by ultrasound.

In summary, we have found ultrasound to be an easy and highly accurate investigation of scrotal pathology. Our accuracy rate agrees closely with other authors (Nachtsheim et al, 1983; Pintauro et al, 1985; Rifkin et al, 1985, Tackett et al, 1986). We feel its advantages over clinical examination alone have been demonstrated by the results of this series. We advocate the use of ultrasonography in all patients referred to a urological unit with scrotal symptoms or signs and feel that this is justified by the tumour detection rate illustrated in this series.

ACKNOWLEDGMENTS

We are grateful to Mr P Clark and Mr R E Williams for referring their patients, to Dr C K Anderson for invaluable help with the pathological specimens and to Miss J. M Seymour for preparing the manuscript

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1987, *The British Journal of Radiology*, *60*, 655–660 JULY 1987

# Ultrasonographic patterns of focal hepatic and splenic lesions in Hodgkin's and non-Hodgkin's lymphoma

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(*Received January 1986 and in revised form October 1986*)

## ABSTRACT

The sonographic patterns of focal lesions of the liver and spleen in 26 patients with Hodgkin's disease and non-Hodgkin's lymphoma are described. Thirteen out of 19 hepatic lesions and nine out of 11 splenic lesions corresponded to a nodular lymphomatous involvement. The remaining cases involved benign focal lesions of the liver and spleen The vast majority of the hepatic and splenic lymphomatous nodules had a hypoechoic pattern with indistinct edges. Target lesions of the liver were seen only in non-Hodgkin's lymphoma Echogenic lymphomatous nodules could not be detected. All echogenic lesions (three) were biopsied and found to be benign Whereas a focal liver involvement almost always occurred in combination with hepatomegaly, only two out of nine patients with splenic foci had splenomegaly The response of hepatic and splenic lymphoma to chemotherapy is described from follow-up examinations in 11 cases. Because of the inherent risk of over-treatment of the false positive interpretation of hepatic nodules, the large-scale use of needle biopsy in sonographically equivocal lesions is strongly advocated

During the late stages of Hodgkin's and non-Hodgkin's disease, the liver and spleen are frequently involved by lymphoma (Levitan et al, 1961; Rosenberg et al, 1961; Carroll & Ta, 1980; Harell, 1981). Pathologically, the most common type of hepatic and splenic involvement is a diffuse distribution of lymphoma which can only be diagnosed by microscopy (Wraight & Symmers, 1966) and not by any of the imaging methods.

At present, very little information is available about the rare form of nodular lymphoma involvement of the liver and spleen (Cosgrove, 1979; Carroll & Ta, 1980; Ginaldi et al, 1980). This paper describes the sonomorphology of focal lesions of the liver and spleen in Hodgkin's and non-Hodgkin's lymphoma and examines their response to chemotherapy.

## PATIENTS AND METHODS

Over a period of 2 years, 256 patients with Hodgkin's (89 patients) and non-Hodgkin's lymphoma (167 patients) were examined by ultrasound as a part of initial staging or restaging. In 26 patients (11 women and 15 men), focal lesions of the liver and spleen were detected sonographically. The patients' ages ranged from 12 to 74 years with a mean of 46 years. Histological verification of the focal lesions was carried out in 19 cases by biopsy, operation or autopsy. In the remaining cases, short-term changes in the size of the foci after chemotherapy clearly indicated their lymphomatous nature so that verification by biopsy was not considered to be necessary. Examinations were performed using real-time scanners with 2.4 MHz and 5 0 MHz transducers (SAL 20 A and SAL 50 A, Toshiba).

## RESULTS

### *Focal lesions of the liver*

Nineteen patients (7.4%) demonstrated focal hepatic lesions on the sonogram. However, only 13 out of 19 patients with hepatic lesions were shown to have lymphomatous involvement of Hodgkin's ($n = 4$) or non-Hodgkin's ($n = 9$) disease The remaining six cases involved benign focal liver lesions. The incidence of focal lymphomatous involvement was 4.5% in the Hodgkin's group and 5.4% in the non-Hodgkin's group. Diagnosis was proven in seven cases by biopsy, in four cases by autopsy, and in eight cases by sonographic follow-up indicating short-term changes under chemotherapy.

(*a*) *Focal lymphomatous involvement of the liver* ($n = 13$). Three different sonographic patterns were observed.

1 Hypoechoic lesions ($n = 10$): this echo pattern was the most common one and was observed in three patients with Hodgkin's and seven patients with non-Hodgkin's disease. The lesions were usually round or oval and well defined with smooth borders, ranging in size from 1.5 cm to 7.0 cm (Figs 1 and 4). Multiple foci of different sizes were detected in seven patients while only three patients had a single lesion. The right and left liver lobes were affected with equal frequency In three cases, target lesions were observed in addition.

2 Target lesions ($n = 4$): echogenic foci surrounded by a hypoechoic rim were observed in only four patients with non-Hodgkin's lymphoma and were multiple in all cases (Fig. 2). In three cases hypoechoic lesions were found in addition. The size of the target lesions ranged from 3.0 cm to 4.0 cm

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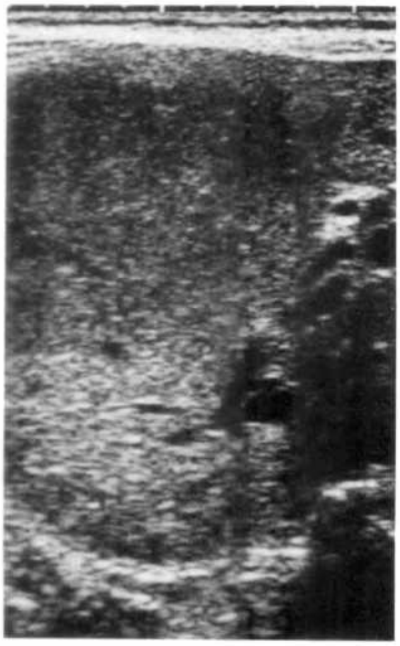

Fig. 1.

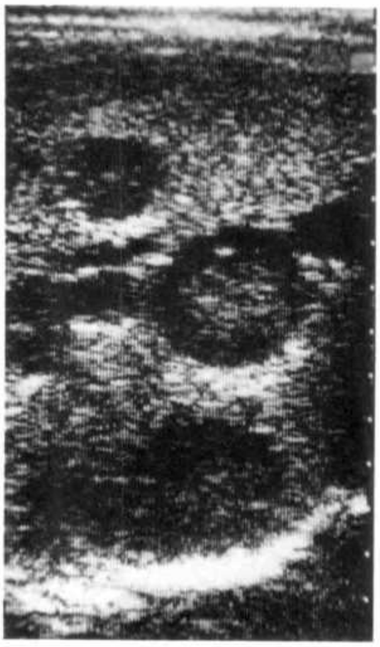

Fig. 2.

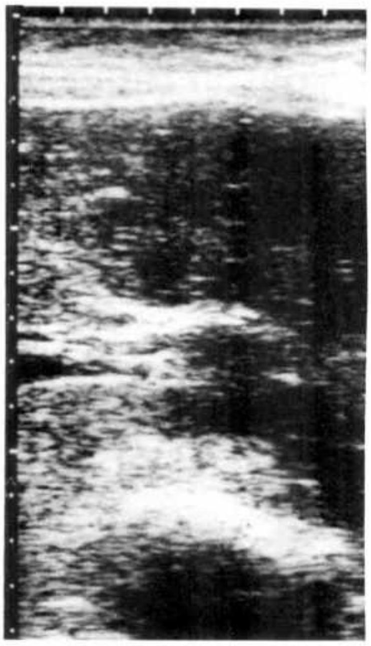

Fig. 3.

Fig. 1. Transverse sonogram of the right hepatic lobe demonstrates a hypoechoic, indistinctly marginated lesion, 7 cm in diameter, displacing the right branch of the portal vein. Non-Hodgkin's lymphoma.

Fig. 2. Transverse sonogram of the right hepatic lobe showing multiple echogenic foci surrounded by hypoechoic borders. Non-Hodgkin's lymphoma.

Fig. 3. Transverse sonogram of the liver showing hypoechoic infiltration of the whole of the left lobe with tongue-shaped branches extending towards the porta hepatis. Hodgkin's disease.

3 Extensive hypoechoic liver infiltrates ($n = 2$): "geographic" patterns of the liver parenchyma were observed in only two cases (one Hodgkin's, one non-Hodgkin's). In one patient there was a hypoechoic infiltration of the left lobe with tongue-shaped branches towards the porta hepatis (Fig. 3). In the second case, initially only a narrow subcapsular rim was observed from which, however, an extensive infiltration of the right lobe of the liver and upper pole of the left kidney had developed within 2 months.

Seven out of the 13 patients with focal lymphomatous involvement of the liver had pronounced hepatomegaly (span in the right MCL: 14–22 cm). Moderate enlargement of the liver was found in three patients whereas liver size remained normal in another three. Porta hepatis adenopathy could not be detected in any patient.

Four out of 13 patients with lymphomatous hepatic lesions had had splenectomy at the time of initial sonographic diagnosis. Four of the remaining 9 patients revealed additional focal splenic involvement. In two cases there was splenomegaly with a homogeneous echo texture; in three cases the spleen was normal. Further manifestations of intra-abdominal lymphoma were registered in only two patients. In both cases there were grossly enlarged para-aortic lymph nodes.

A goup of nine patients with hepatic lymphoma underwent sonographic follow-up studies during and after chemotherapy (Fig. 4), with an observation time ranging from 4 weeks to 24 months (mean 9 months). Four patients were lost to follow-up due to fulminant progress of the disease ($n = 2$) or treatment in another hospital ($n = 2$).

Changes in the ultrasonographic pattern such as are occasionally observed in metastasis as a result of necrosis or a liquefaction were not detected in focal lymphomatous lesions of the liver. Only the change in size of the hepatic lesions was variable and corresponded closely with the response, or lack of response, to chemotherapy (Table I).

*(b) Benign focal lesions of the liver* ($n = 6$). In six lymphoma patients, sonographically guided fine-needle biopsy revealed benign focal lesions. The sonomorphology and final diagnosis of these lesions are outlined in Table II.

*Focal lesions of the spleen*

Focal lesions of the spleen were detected in 11 patients with lymphoma. In nine of these (six

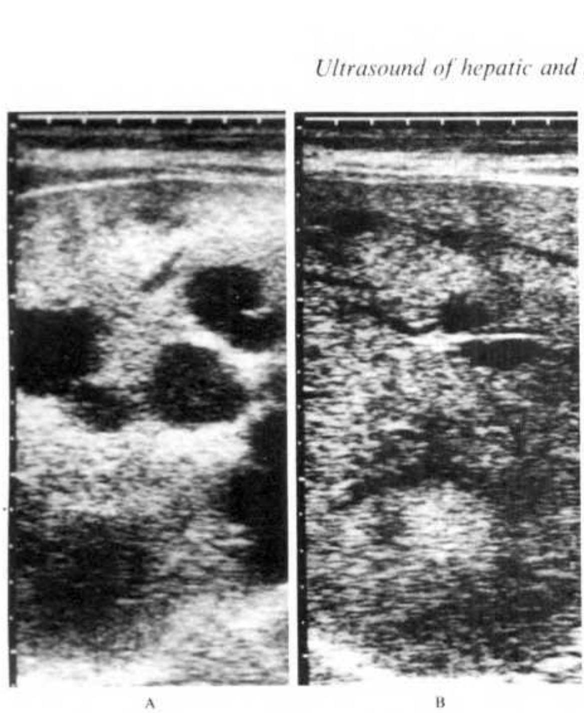

FIG. 4.

(A) Transverse sonogram through the right lobe of the liver showing multiple hypoechoic lesions up to 3.5 cm in diameter. Non-Hodgkin's lymphoma. (B) Six weeks later, after one course of chemotherapy. Only a few hypoechoic lesions, up to 1.0 cm in diameter, are evident.

Hodgkin's, three non-Hodgkin's) they corresponded to a nodular lymphomatous involvement. Diagnosis was confirmed by operation in five cases, and by autopsy in two. In the remaining two, organ involvement was verified by short-term changes in the size of the splenic nodules under chemotherapy. Because of additional liver foci (Stage IV), splenectomy was not carried out.

In two cases an accessory spleen was mistakenly interpreted as a focal lymphomatous infiltration. In both cases there was broad contiguity with the spleen. This finding, combined with a markedly reduced echogenicity as compared with the adjacent spleen, was responsible for the impression of a focal mass (Fig. 6). The final diagnosis was made in one patient by operation, in the second by scintigraphy.

Two different echo-patterns of nodular splenic involvement were observed.

1. Hypoechoic focal lesions ($n = 7$): this echo pattern was the most frequent and was observed in seven out of the nine patients (four Hodgkin's, three non-Hodgkin's). In contrast to the hypoechoic liver foci, the splenic foci had indistinct and irregular edge contours (Fig. 7). They were all multiple, ranging in size from 0.5 cm to 4.0 cm. In one case additional target lesions were found.
2. Target lesions ($n = 3$): echogenic foci surrounded by a hypoechoic rim were observed in three patients (two Hodgkin's, one non-Hodgkin's) (Fig. 8). The size of the foci ranged from 2.0 cm to 4.0 cm in diameter.

Bulging of the splenic capsule caused by small foci on the surface or by larger foci in the centre was found in six out of the nine patients (Fig. 7). The spleen was enlarged in only two out of the nine patients. Splenic hilar adenopathy was found in only one patient.

In four out of the nine patients with nodular splenic involvement, simultaneous focal liver lesions were detected sonographically. Two more patients revealed para-aortic adenopathy.

Since most of our patients underwent splenectomy, only two remained for sonographic follow-up studies of focal splenic lesions under chemotherapy. One patient responded very favourably, the lesions disappearing completely after only one course of chemotherapy. In the second case, there was enlargement of the lesions during therapy.

## DISCUSSION

### *Focal lesions of the liver*

Liver involvement can be detected histologically in 50–60% of the advanced stages of Hodgkin's and non-Hodgkin's lymphoma (Levitan et al, 1961; Rosenberg et al, 1961; Blendis et al, 1970). Sonographic detection of involvement can be difficult because of the predominantly diffuse infiltration of the liver parenchyma by lymphoma cells (Wraight & Symmers, 1966).

TABLE I

ULTRASONOGRAPHIC EVALUATION OF CHEMOTHERAPEUTIC RESPONSE IN HEPATIC LYMPHOMA ($n = 9$)

| Reaction of the hepatic lymphomatous nodules | Change in liver size | Clinical course |
|---|---|---|
| Complete regression ($n = 2$) | Hepatomegaly regressive ($n = 2$) | Full remission ($n = 2$) (observation time 4 months–2 years) |
| Partial regression ($n = 3$) | Unchanged hepatomegaly ($n = 1$) | Partial remission (relapse after 4 months) |
| | Hepatomegaly regressive ($n = 1$) | Partial remission (relapse after 6 months) |
| | Liver size constantly normal ($n = 1$) | Partial remission (relapse after 8 months) |
| Stationary size ($n = 1$) | Unchanged hepatomegaly | Stationary disease (observation time 7 months) |
| Increase in size ($n = 3$) | Increasing hepatomegaly ($n = 1$)<br>Liver size constantly normal ($n = 2$) | Progression ($n = 3$) |

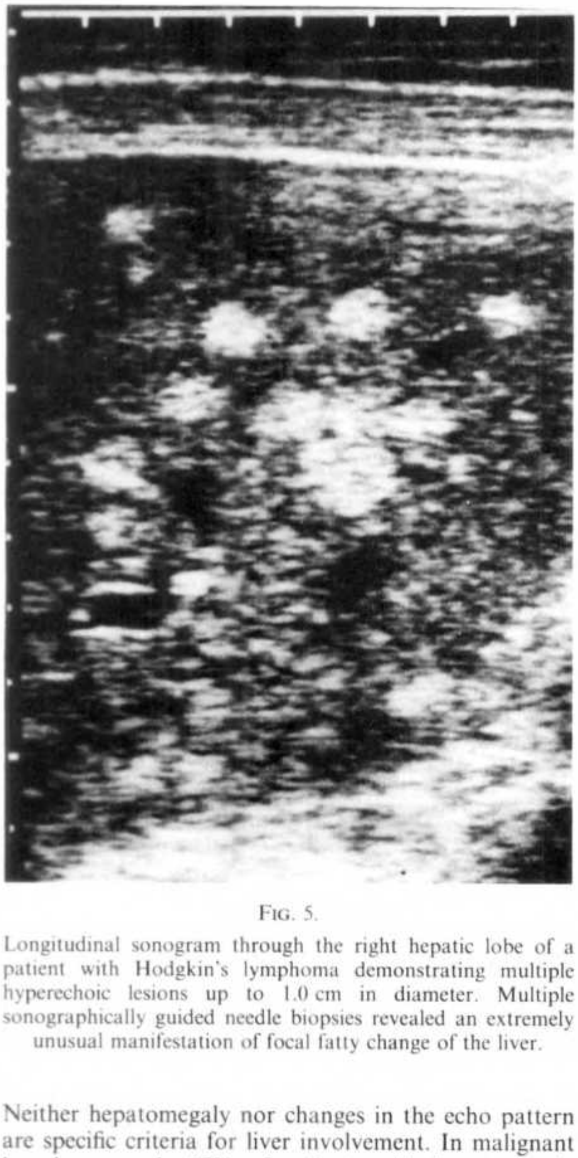

FIG. 5.

Longitudinal sonogram through the right hepatic lobe of a patient with Hodgkin's lymphoma demonstrating multiple hyperechoic lesions up to 1.0 cm in diameter. Multiple sonographically guided needle biopsies revealed an extremely unusual manifestation of focal fatty change of the liver.

Neither hepatomegaly nor changes in the echo pattern are specific criteria for liver involvement. In malignant lymphoma, only 57% of patients with hepatomegaly have histologically proven liver involvement (Rosenberg et al, 1961). On the other hand, there may well be lymphomatous infiltration of a normal-sized liver (Levitan et al, 1961). Analysis of the echo pattern structure is not very helpful as it is dependent on a variety of factors, such as changes in the liver cells induced by chemotherapy (Carroll & Ta, 1980).

Sonographically detectable focal lesions in lymphoma patients are rare. In our study, only 4.5% of Hodgkin's and 5.4% of non-Hodgkin's lymphoma displayed a nodular lymphomatous involvement. These results correspond to the study of Ginaldi et al (1980), who found an incidence of 5.8% in Hodgkin's and 5% in non-Hodgkin's lymphoma.

The sonographic appearance of the hepatic foci is relatively uniform. Among our patients, the vast majority of the liver nodules (10 out of 13) had a hypoechoic pattern with indistinct and irregular edges (Figs 1, 4). The extensive "geographical" infiltration of the liver parenchyma (two out of 13) can be seen as a variation of the hypoechoic nodules (Fig. 3) which occasionally may pass beyond the liver and spread to other organs. Target lesions are also rare (four out of 13). As in the study of Ginaldi et al (1980), they are found only in non-Hodgkin's lymphoma (Fig. 2). In contrast to these authors, we were unable to detect echogenic liver foci in our patients. All three of our echogenic liver lesions were biopsied and were found to be benign (Table II; Fig. 5).

Focal lymphomatous involvement of the liver occurred mostly in combination with hepatomegaly (10 out of 13). On the other hand, porta hepatis adenopathy was not detected in any patient. Four out of the nine patients who had not undergone splenectomy showed focal lymphomatous involvement of the spleen and the liver.

Three different types of response of focal liver infiltrates to chemotherapy were observed (Table I):

(a) reduction in size ($n = 3$) or complete regression ($n = 2$);
(b) enlargement ($n = 3$);
(c) no change in size ($n = 1$).

The echo pattern of the focal liver lesions did not change with chemotherapy. The size of the liver changed in proportion to the degree of infiltration, *i.e.* where there was a reduction of the foci there was also reduction of pre-existent hepatomegaly. There was also good correlation between the clinical course and the change in size of the liver foci in all cases, thus allowing monitoring of therapeutic response to different combinations of drugs. However, it must be kept in mind that even complete regression of liver foci does not exclude microscopic liver infiltration.

Focal, poorly marginated hypoechoic masses are a typical feature of lymphomatous hepatic involvement but not specific enough to be differentiated from other benign or malignant liver lesions.

The incidence of nodular liver involvement in malignant lymphoma (5%) approximately corresponds to that of benign liver lesions in the general population (Taylor & Richman, 1983). In our series, six out of 19 focal lesions turned out to be benign. Thus there is always the possibility of false positive interpretation of sonographic examinations with the inherent risk of over-treatment. The large-scale use of fine-needle biopsy in sonographically equivocal lesions is strongly advocated. In our experience, small liver cysts less than 1.5 cm in diameter can hardly be differentiated from hypoechoic lymphomatous foci because of their artificial internal echoes. Echogenic liver nodules in patients with malignant lymphoma are very likely to be benign. All three echogenic liver lesions among our

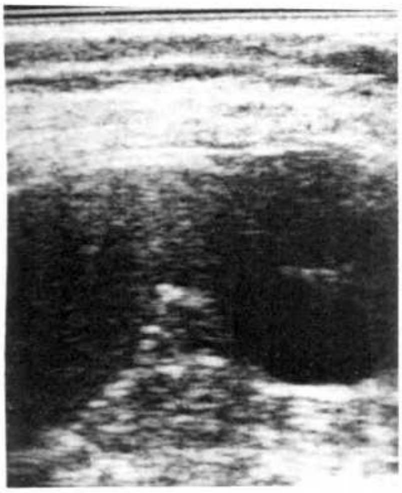

Fig. 6.

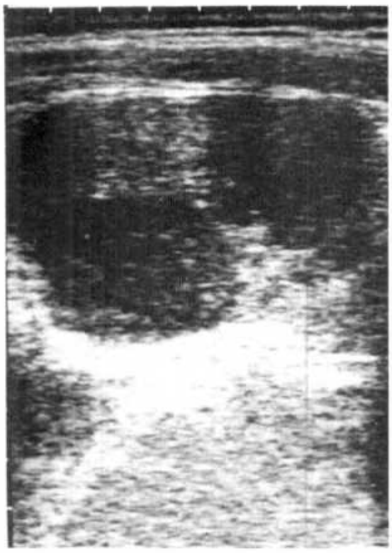

Fig. 7.

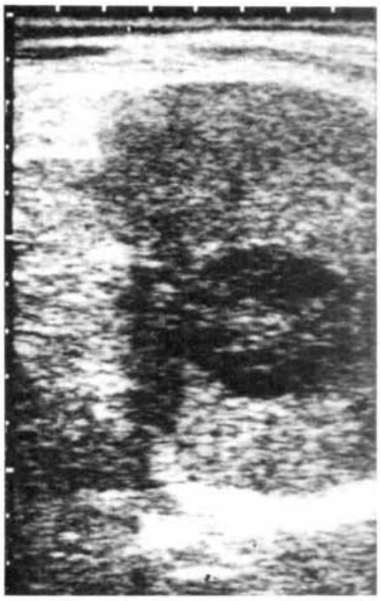

Fig. 8.

Fig. 6. Longitudinal sonogram through the spleen of a patient with non-Hodgkin's lymphoma showing a large hypoechoic mass in the lower splenic pole, interpreted as focal lymphomatous infiltration. Splenectomy revealed an accessory spleen only.

Fig. 7. Longitudinal sonogram of the spleen showing multiple hypoechoic lesions with bulging of the splenic capsule. Hodgkin's disease.

Fig. 8. Longitudinal sonogram of the spleen showing a hypoechoic lesion with scattered echogenic foci. This lesion was due to Hodgkin's lymphoma.

patients underwent fine-needle biopsy and were histologically proven to be benign (Table II; Fig. 5).

*Focal lesions of the spleen*

Sonographic diagnosis of splenic involvement in Hodgkin's and non-Hodgkin's lymphoma raises similar problems. Detection of splenomegaly is not reliable evidence of splenic involvement. Only two-thirds of the patients with Hodgkin's lymphoma and splenomegaly had histologically proven splenic infiltration at the time of splenectomy (Harell, 1981). Again, a normal-sized spleen does not exclude the possibility of splenic involvement (Zornoza & Ginaldi, 1981). Analysis of the splenic echo texture is not particularly helpful as it is dependent on so many other factors, such as the vascularity of the organ or reactive changes (Carroll & Ta, 1980).

Sonographically detectable focal splenic lesions in lymphoma patients are rare. Firm evidence of the incidence of focal splenic involvement is not available

TABLE II

SONOMORPHOLOGY AND FINAL DIAGNOSIS OF SIX BENIGN HEPATIC LESIONS IN LYMPHOMA PATIENTS

| Case | Age (years), Sex | Sonomorphology | Final diagnosis (needle biopsy) |
|---|---|---|---|
| 1 | 41, M | Multiple hypoechoic, irregularly marginated lesions (up to 2 cm) | Multiple liver cysts |
| 2 | 60, F | Hypoechoic, irregularly marginated lesion (2.5 cm) in the liver with increased echogenicity | Focal non-fatty area in a fatty liver induced by chemotherapy |
| 3 | 62, M | Hypoechoic lesion (2 cm) with bulging of the liver contour | Haemangioma |
| 4 | 61, F | Multiple hyperechoic lesions (up to 2.5 cm) | Multiple haemangiomas |
| 5 | 37, M | Multiple hyperechoic lesions (up to 1 cm) (Fig. 5) | Multiple foci of fatty change in the liver |
| 6 | 54, F | Hyperechoic, irregularly marginated lesion (7 cm) with bulging of the liver contour | Haemangioma |

because, as in the study by Carroll and Ta (1980), many of our patients underwent splenectomy as part of a staging laparotomy. The echo patterns of the splenic nodules is similar to that of hepatic lymphomatous foci. The vast majority of the splenic foci (seven out of nine) were hypoechoic and indistinctly marginated (Fig. 7) Target lesions (Fig 8) were observed in only three patients, two of whom suffered from Hodgkin's disease. Echogenic lymphomatous infiltrates were likewise not detected in the spleen.

Whereas focal liver involvement almost always occurred together with enlargement of the organ (10 out of 13), only two out of the nine patients with splenic foci had splenomegaly. Bulging of the organ contours was frequently observed in splenic lymphoma (six out of nine) (Fig. 7), while even superficially situated lymphomatous liver nodules did not cause the liver contours to bulge. The high incidence of simultaneous nodular involvement of the liver and spleen (four out of nine) has already been emphasised.

Although the small number of patients with follow-up studies (two) does not permit a conclusive statement, splenic lymphomatous nodules seem to react to chemotherapy in the same way as liver foci.

As in the liver, the sonographic appearance of splenic lymphomatous infiltrates is non-specific so that differentiation from other benign or malignant splenic foci such as cysts, haematomas, abscesses, metastases or accessory spleens may be difficult However, the overall incidence of focal lesions of the spleen is so low (~ 0.1%) that nodule formation in a given lymphoma patient almost always represents lymphomatous involvement.

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# A comparison of technetium-99m-thiodiglycolic acid and iodine-123-hippuran in the evaluation of equivocal upper urinary tract obstruction

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(*Received September 1986*)

ABSTRACT

In a comparative trial, 21 patients (mean age 43 (range 19–66) years) with dilated upper urinary tracts underwent diuresis renography with both $^{123}$I-hippuran and the experimental agent, $^{99}$Tc$^{m}$-thiodiglycolic acid (TDG) Deconvolution analysis of the derived renograms was also performed and the transit times were calculated Excellent agreement was found between results with the two radiopharmaceuticals. There was complete agreement in interpretation of the response to diuresis with both agents and 84% agreement in the transit time estimations. Good images were produced with both agents and $^{99}$Tc$^{m}$-TDG is considered to be a useful alternative to $^{123}$I-hippuran.

The investigation of equivocal upper urinary tract obstruction is a problem which has concerned clinical urologists for many years. The distinction between obstructed and dilated but non-obstructed collecting systems is important, as obstruction may lead to deteriorating renal function, which is preventable by surgical intervention. Alternatively, in the non-obstructed kidneys conservative treatment may be undertaken with the expectation of preservation of existing renal function. Two renographic techniques have been developed independently in recent years in an attempt to distinguish between obstruction and non-obstruction. Both are non-invasive and simple to perform.

Diuresis renography has been shown to be of significant value in the distinction between obstructed and non-obstructed upper urinary tracts (O'Reilly et al, 1978a, b; Koff et al, 1979; Kreuger et al, 1980, O'Reilly et al, 1981; Stage & Lewis, 1981) and provides good correlation with the morphological changes of upper urinary tract obstruction (Lupton et al, 1979; English et al, 1982). This method involves the interpretation of the response to a diuresis evoked by frusemide (O'Reilly et al, 1986). According to the renogram pattern, patients may be regarded as one of four types (Fig. 1).

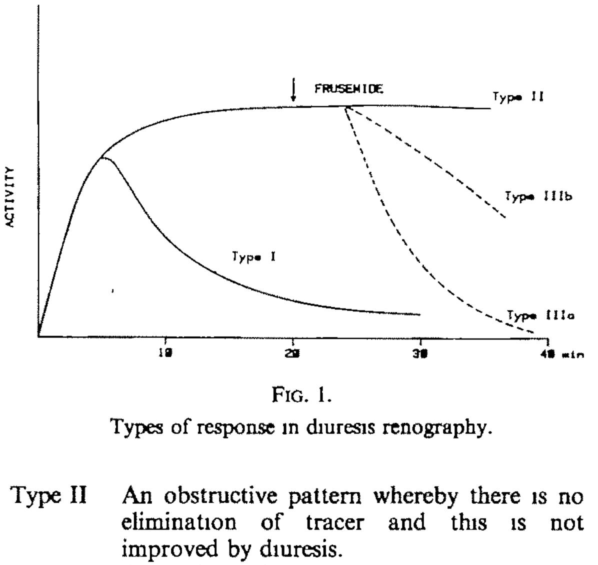

FIG. 1.

Types of response in diuresis renography.

| | |
|---|---|
| Type I | A normal renogram. |
| Type II | An obstructive pattern whereby there is no elimination of tracer and this is not improved by diuresis. |
| Type IIIa | An initially obstructive curve which, following diuresis, shows rapid and complete elimination of tracer, indicating a non-obstructed, hypotonic collecting system. |
| Type IIIb | An obstructive curve which, following diuresis, shows only slow and incomplete elimination of tracer. This is an equivocal response and in some cases may indicate partial impedance to flow or a kidney functioning too poorly to respond maximally to the diuretic. |

The second method involves the estimation of parenchymal transit times and relies on the ability of the gamma-camera computer system to distinguish between regions of interest comprising the renal parenchyma and the collecting system. Deconvolution analysis of the respective activity–time curves enables the radionuclide transit times for the whole kidney and renal parenchyma to be determined. In significant obstruction, both the whole-kidney and parenchymal transit times are prolonged, while in the non-obstructed kidney the parenchymal transit time is normal (Kenny et al, 1975; Whitfield et al, 1977, 1978) Both techniques also enable accurate and objective measurement of the divided renal function.

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In previous work we have reported results with an experimental radiopharmaceutical, $^{99}$Tc$^{m}$-thiodiglycolic acid (TDG), which was developed by Amersham International PLC for the evaluation of renal function. It was shown to be cleared from plasma at almost twice the rate of DTPA and to produce excellent images of the renal system with uptake ratios approaching those of hippuran (Bevis et al, 1983; Nowotnik et al, 1985) Deconvolution analysis, however, showed that the transit time of TDG was longer than that of other agents (Bevis et al, 1984), possibly because a fraction becomes bound to renal parenchyma.

This could affect the interpretation of dynamic studies and might lead to a greater number of equivocal responses with diuresis renography. The purpose of this study was therefore to evaluate the effectiveness of TDG in the assessment of abnormal upper urinary tract dynamics, and to compare the results with those obtained using $^{123}$I-hippuran.

## MATERIALS AND METHODS

Twenty-one patients referred for gamma-camera renography underwent studies with 12 MBq $^{123}$I-hippuran ($^{123}$I obtained from the Atomic Energy Research Establishment, Harwell) followed after an interval of 2–4 days by a further study performed with 75 MBq $^{99}$Tc$^{m}$-TDG (kit produced experimentally by Amersham International PLC). The dose administered in each case was that which would normally be given for a routine diagnostic study, having regard to the cost, the absorbed radiation dose and the renal uptake. All the subjects had dilatation of one or both of the upper urinary tracts on intravenous urography. There were 19 men and two women, with a mean age of 43 (range 19–66) years.

The patients were fully hydrated and gamma-camera renograms were acquired in a standard manner. The gamma camera (Elscint, Dymax LF) was positioned for a posterior view of the kidneys and bladder and, following the injection of the radiopharmaceutical, six to eight 5 min analogue images were acquired. At the same time, the computer system (multiterminal Medical Data Systems A$^{2}$) stored 20 s images for a period of 30–40 min. All 21 patients received an injection of 0.5 mg/kg body weight of frusemide at 18–22 min. Using the computer-stored images, regions of interest were defined for each kidney, background and bladder, and background-corrected renogram curves were derived. The sensitivity of the gamma camera to each radionuclide had previously been determined by measuring the response to a known activity within a phantom which simulated a kidney at a fixed depth. The renogram curves were, thus, crudely calibrated and expressed as percentage of the dose injected (O'Reilly et al, 1986).

Relative renal function was computed from the data between 1 min and the renogram peak or, in the absence of a peak, between 1 min and 5 min

Deconvolution analysis was performed on the renograms obtained with both $^{123}$I-hippuran and $^{99}$Tc$^{m}$-TDG for all 21 patients. From the computer-stored images, regions of interest were defined for the whole kidney, renal parenchyma and a blood region. The region representing renal parenchyma was identified visually by using a joystick to define it on summed early images and then excluding any pixels suspected of being in the renal pelvis because of activity on later summed images. The most suitable site for the blood region was found to be above the renal areas, which included the base of the heart. Activity–time curves were derived for each region up to the time when frusemide was given Deconvolution analysis was applied to the whole kidney and parenchymal regions using the matrix algorithm (O'Reilly et al, 1986). From the resulting retention functions the whole-kidney and parenchymal mean transit times were calculated.

## RESULTS

Table I shows the age and relative renal function figures obtained with both $^{99}$Tc$^{m}$-TDG and $^{123}$I-hippuran in the 21 patients. The sets of values are highly correlated ($r = 0.98$). The mean difference between pairs was $1.95 \pm 3.65$ (mean ± standard deviation). Wilcoxon's matched-pairs signed ranks sum test indicated that the difference was not significant at the 2% level.

TABLE I

RELATIVE RENAL FUNCTION

| Case No | Age (years) | Sex | Relative function of left kidney* | |
|---|---|---|---|---|
| | | | $^{99}$Tc$^{m}$-TDG | $^{123}$I-hippuran |
| 1 | 32 | M | 84 | 86 |
| 2 | 41 | M | 47 | 43 |
| 3 | 40 | F | 36 | 38 |
| 4 | 19 | M | 15 | 11 |
| 5 | 21 | M | 56 | 56 |
| 6 | 28 | M | 50 | 45 |
| 7 | 66 | M | 59 | 63 |
| 8 | 36 | M | 37 | 35 |
| 9 | 41 | M | 21 | 18 |
| 10 | 45 | M | 19 | 21 |
| 11 | 60 | F | 62 | 53 |
| 12 | 51 | M | 67 | 61 |
| 13 | 55 | M | 55 | 57 |
| 14 | 53 | M | 47 | 47 |
| 15 | 50 | M | 68 | 62 |
| 16 | 52 | M | 34 | 37 |
| 17 | 57 | M | 47 | 45 |
| 18 | 46 | M | 54 | 52 |
| 19 | 62 | M | 43 | 38 |
| 20 | 32 | M | 40 | 39 |
| 21 | 34 | M | 51 | 44 |

*Expressed as a % of total renal function

TABLE II

RADIONUCLIDE PARENCHYMAL MEAN TRANSIT TIMES (MIN) AND RESPONSE TO DIURESIS (IN PARENTHESIS)

| Case No. | $^{99}$Tc$^{m}$-TDG | | $^{123}$I-hippuran | |
|---|---|---|---|---|
| | Left kidney | Right kidney | Left kidney | Right kidney |
| 1 | 2.7 (I) | 7.5 (II) | 1.8 (I) | 6.1 (II) |
| 2 | 3.0 (I) | 3.0 (IIIa) | 2.0 (I) | 2.3 (IIIa) |
| 3 | 2.9 (IIIa) | 2.2 (I) | 2.3 (IIIa) | 2.1 (I) |
| 4 | 7.8 (IIIb) | 2.9 (I) | 12.7 (IIIb) | 2.6 (I) |
| 5 | 3.0 (I) | 1.8 (IIIa) | 1.9 (I) | 1.9 (IIIa) |
| 6 | 2.7 (IIIa) | 2.6 (I) | 2.9 (IIIa) | 2.0 (I) |
| 7 | 3.5 (I) | *1.9 (II) | 1.5 (I) | *1.8 (II) |
| 8 | *†2.6 (IIIb) | 2.3 (I) | †4.2 (IIIb) | 1.7 (I) |
| 9 | *4.9 (IIIa) | 3.8 (I) | *5.7 (IIIa) | 2.1 (I) |
| 10 | †4.7 (IIIb) | 2.4 (I) | *†2.5 (IIIb) | 1.6 (I) |
| 11 | 3.1 (I) | *3.3 (IIIb) | 2.1 (I) | *2.4 (IIIb) |
| 12 | 3.2 (IIIa) | 1.7 (I) | 2.2 (IIIa) | 1.8 (I) |
| 13 | *†4.7 (IIIa) | *8.1 (IIIa) | †2.5 (IIIa) | *4.6 (IIIa) |
| 14 | *†5.0 (IIIa) | 4.0 (I) | †1.7 (IIIa) | 2.2 (I) |
| 15 | 3.1 (I) | *3.8 (IIIb) | 2.0 (I) | *2.2 (IIIb) |
| 16 | *†4.6 (IIIa) | 4.1 (IIIa) | †2.5 (IIIa) | 2.1 (IIIa) |
| 17 | 2.4 (IIIa) | 3.0 (I) | 2.6 (IIIa) | 2.1 (I) |
| 18 | 3.0 (I) | 4.2 (IIIa) | 1.9 (I) | 2.6 (IIIa) |
| 19 | 4.6 (IIIb) | 7.8 (II) | 5.1 (IIIb) | 6.4 (II) |
| 20 | 9.4 (IIIb) | 2.3 (IIIa) | 7.5 (IIIb) | 1.8 (IIIa) |
| 21 | 4.2 (IIIa) | 3.2 (I) | 2.2 (IIIa) | 2.0 (I) |

Normal parenchymal mean transit time $< 3.6$ min for hippuran and $< 4.2$ min for TDG.

*Discrepancy between parenchymal mean transit time and response to diuresis

†Discrepancy in transit-time estimation between TDG and hippuran.

The effect of diuresis was assessed independently by two observers who classified the curves according to the scheme indicated in Fig. 1. There was no disagreement between observers, and the results obtained for the 42 kidneys are shown in Table II. In all cases the response was the same with both agents. Seventeen kidneys gave a Type I response, three kidneys a Type II response, 14 kidneys a Type IIIa response and eight kidneys a Type IIIb response.

Mean parenchymal and whole-kidney transit times were compared with the times previously found in normal kidneys (Bevis et al, 1984). We have taken the upper limit of normal of the mean transit time as the mean plus two standard deviations, giving normal values for $^{123}$I-hippuran and $^{99}$Tc$^{m}$-TDG parenchymal transit times of less than 3.6 min and 4.2 min respectively. The results obtained in all 42 kidneys are also shown in Table II.

In this study all 17 kidneys found to give a Type I (normal) response to diuresis renography had a normal parenchymal mean transit time with both hippuran and TDG.

Of the 14 kidneys with a Type IIIa (hypotonic) response, 12 had a normal parenchymal mean transit time with hippuran and nine had a normal parenchymal mean transit time with TDG.

Of the three kidneys which gave a Type II (obstructed) response with both hippuran and TDG, one had normal parenchymal mean transit times with both agents.

Of the eight Type IIIb (equivocal response) patients, three had normal parenchymal mean transit times with hippuran, and three out of eight had normal parenchymal mean transit times with TDG

The agreement between TDG and hippuran in the evaluation of equivocal obstruction was good. Using diuresis renography there was agreement in all 42 kidneys. Using deconvolution analysis and transit-time estimations there was agreement in 37 out of the 42 kidneys (84%). In all cases good diagnostic images were obtained with both agents (Figs 2, 3).

## DISCUSSION

Iodine-123-hippuran has for some years been considered the agent of choice for evaluating renal function by gamma-camera renography. It produces high-resolution images and reliable renograms with low background and a low radiation dose to the patient (O'Reilly et al, 1977). It is, however, both expensive and of limited availability. For these reasons TDG has been investigated as an alternative agent. It has a similar kidney-to-background ratio to hippuran and the advantage that it may be labelled with $^{99}$Tc$^{m}$.

In the investigation of equivocal upper urinary tract obstruction using diuresis renography we found $^{99}$Tc$^{m}$-TDG to be as effective as $^{123}$I-hippuran. The elimination phase of the derived renogram was more prolonged with $^{99}$Tc$^{m}$-TDG than with $^{123}$I-hippuran, but this did not interfere with the interpretation of the renograms.

When diuresis is used, deconvolution analysis can be applied to the renogram only for the period prior to the injection of frusemide, since frusemide invalidates the technique as the system can no longer be considered stationary because of the increased urine flow rate. It has been proposed that radionuclide transit times through the parenchyma can be used as a means of determining whether an obstructive uropathy is affecting nephron function and thus causing an obstructive nephropathy (Whitfield et al, 1978). In our study there was excellent agreement between a Type I (normal) response to diuresis renography and parenchymal mean transit time. There was also agreement in kidneys with a Type IIIa (hypotonic) response. In several cases where the parenchymal mean transit time was considerably prolonged, this was thought to be because of inclusion of some pelvic and calyceal areas within the parenchymal region. If the kidney is rotated, or gross calectasia and pelvic dilatation are present, and/or patient movement occurs, the exclusion of all pelvicalyceal areas from the parenchymal region can be difficult, and the transit-time estimate will be prolonged. In addition, diminished renal function with a lowering

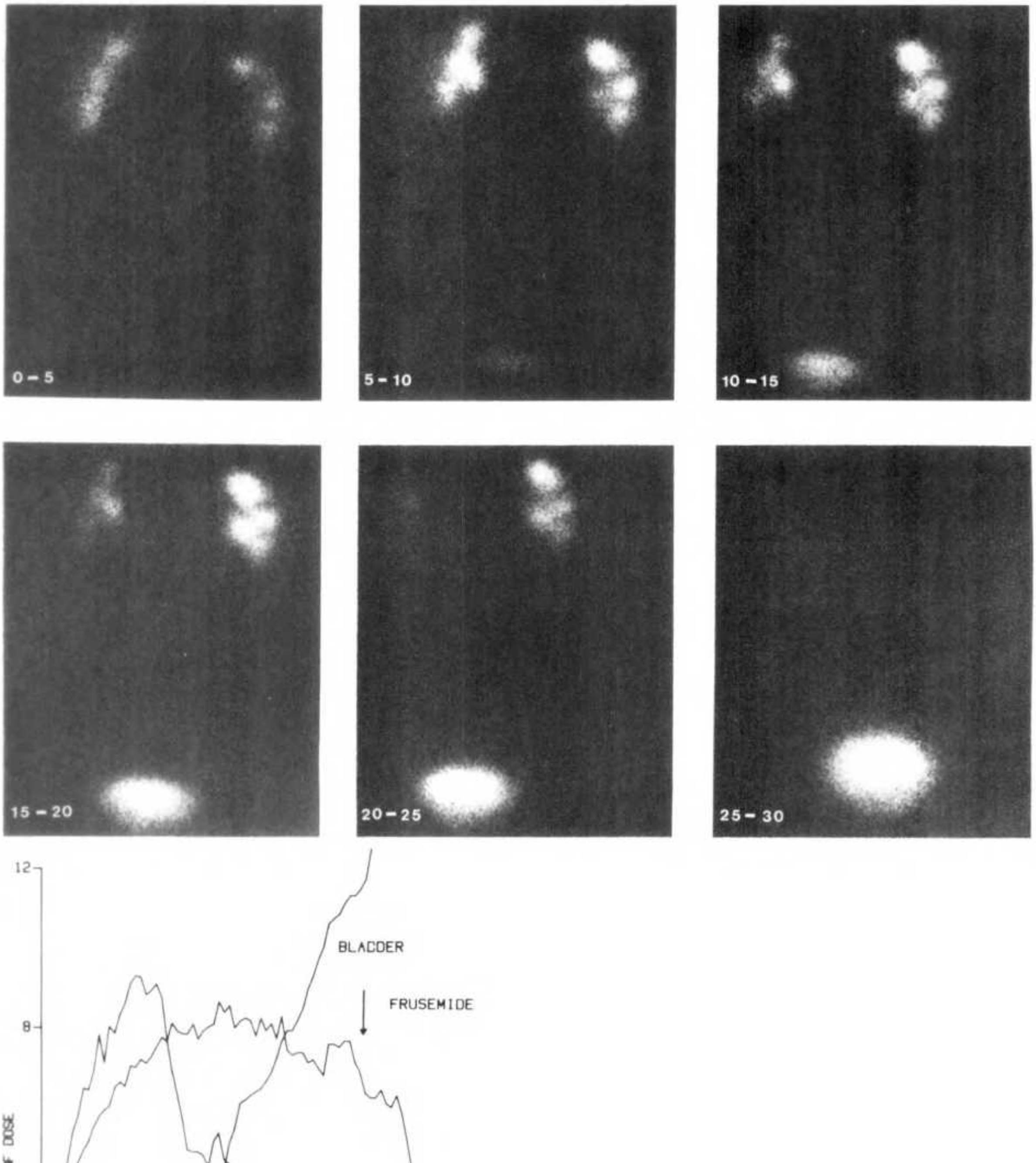

FIG. 2. *Case 5.*
Sequential 5 min analogue images and derived renograms produced with $^{123}$I-hippuran.

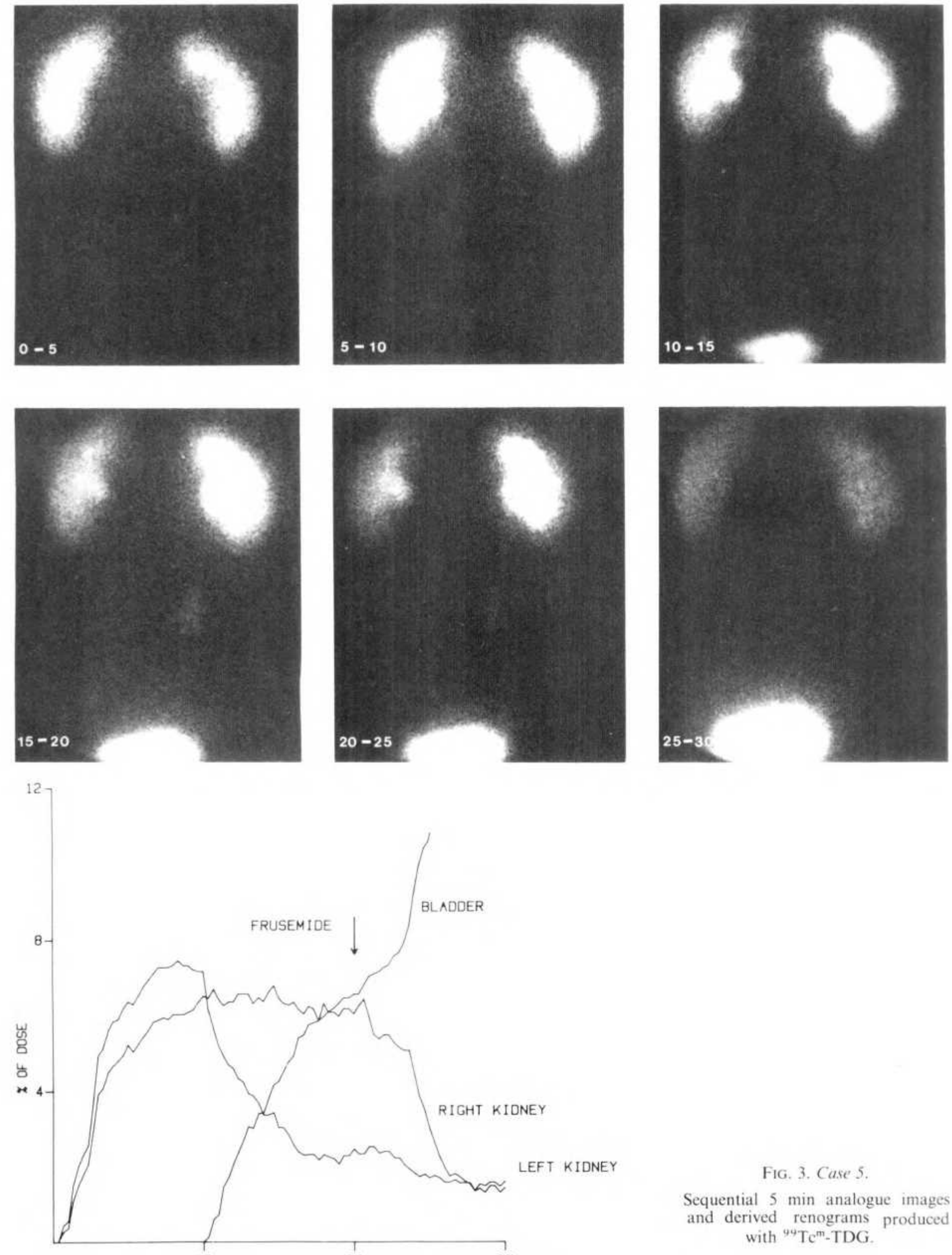

FIG. 3. *Case 5.*

Sequential 5 min analogue images and derived renograms produced with $^{99}$Tc$^m$-TDG.

of the glomerular filtration rate may also prolong the transit time (Farmelant et al, 1979). These factors probably account for the discrepancies which occurred when the results were compared with diuresis renography.

There were only three Type II (obstructed) kidneys in our trial. In the one case (Case 7) where the parenchymal mean transit time was normal, it should be noted that the relative renal function of the obstructed kidney was quite good.

It is not surprising that kidneys with a Type IIIb (equivocal) response showed the least agreement with mean transit-time estimation. All the kidneys in this group had grossly dilated collecting systems and many had some impairment of relative renal function. It may, therefore, sometimes be difficult to interpret the response. Whether the partial response to the diuretic is due to some impedance to flow, or insufficient diuresis due to impaired renal function, possibly combined with a large and compliant pelvis, is not always certain. There was a wide spectrum of parenchymal mean transit times in this group. Any difference between the two radiopharmaceuticals, however, was not obvious.

Technetium-99m-TDG had longer mean transit times than $^{123}$I-hippuran, but this was not a disadvantage. The images produced with 75 MBq $^{99}$Tc$^{m}$-TDG were good and the ease with which the various regions could be delineated was similar with both radiopharmaceuticals. When difficulty occurred it was due to kidney rotation, patient movement or poor function and not to the choice of radiopharmaceutical. The agreement in the relative renal function estimation produced with both agents is gratifying, as it confirms the reliability of the technique. Temporary reduction in function has been known to occur with dilated collecting systems in infective states, and poor perfusion, and interval studies several weeks apart should be considered if any doubt exists.

The principal objective in the management of obstructive uropathy is the preservation of renal function and as a consequence there is a need for accurate and objective divided renal function measurements.

In summary, $^{99}$Tc$^{m}$-TDG proved to be as effective as $^{123}$I-hippuran in the evaluation of the dilated upper urinary tract using renography

ACKNOWLEDGMENT

The authors wish to acknowledge the support of the North West Kidney Research Association which provided a grant to fund this work, and Amersham International PLC which developed and supplied material

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1987, *The British Journal of Radiology*, *60*, 667–670 JULY 1987

# Ultrasonically guided percutaneous inactivation of parathyroid tumours

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(*Received January 1987*)

## ABSTRACT

Four patients with hyperparathyroidism and one parathyroid tumour detected ultrasonically were treated by ultrasonically guided percutaneous injection of ethanol (96%) into the tumour. Normocalcaemia was achieved for a follow-up of 10 months in one patient and of 3 months in another. One patient had a lowered serum calcium level for a follow-up of 5 months. One patient showed no clinical response to treatment but was subsequently shown to have multiglandular involvement at surgical exploration. Ultrasonically guided percutaneous inactivation of solitary parathyroid tumours as an alternative to surgery is discussed.

It is generally agreed that patients with symptoms attributable to hyperparathyroidism (HPT) require surgery (Vant Hoff et al, 1983; Carlew et al, 1985). Non-operative ablation of parathyroid tumours has been employed successfully by Doppman (1980) using angiographic transcatheter techniques, and recently Solbiati et al (1985) have suggested the use of ultrasonically guided ethanol ablation of parathyroid tumours in uraemic patients with secondary HPT.

We present four patients with HPT. In each patient one parathyroid tumour was ultrasonically visualised and the tissue diagnosis verified by ultrasonically guided fine-needle puncture (Gooding et al, 1985; Karstrup et al, 1985, 1986). The parathyroid tumours were all treated by ultrasonically guided percutaneous injection of ethanol.

## METHODS

The ultrasonic scanning was performed with a dynamic 5 MHz curved-array scanner (Picker, LSC 7000) mounted with a needle-steering device for precisely ultrasonically guided puncture.

Tissue diagnosis was obtained using fine-needle (23 gauge, 0.6 mm) aspiration biopsies for cytological examination (Gooding et al, 1985) and parathyroid hormone (PTH) measurement (Karstrup et al, 1985). Histological diagnosis was obtained using a 23-gauge cutting needle (Surecut, TSK Laboratory) (Karstrup et al, 1986).

The injection of alcohol was performed on an outpatient basis with local anaesthesia and under complete ultrasound control. When the needle-tip echo from the fine needle, inserted through the steering device, was seen inside the parathyroid tumour 0.4–1.0 ml of 96% ethanol was injected. The dissemination of the alcohol inside the gland was appreciated by the appearance of fine, dotted echoes spreading over the entire gland (Fig 1). Laryngoscopy was carried out before and after the procedure, which was associated with no, or minimal, discomfort. Informed consent was obtained from all patients.

Parathyroid hormone in the aspirate and in the serum was measured with a C-terminal specific radioimmunoassay (Fischer et al, 1974).

## CASE REPORTS

### *Case 1*

A 36-year-old man presented with biochemical evidence of HPT after a second kidney transplant in 1983. For 8 years he had been treated by haemodialysis for renal failure secondary to chronic glomerulonephritis, diagnosed in 1965.

On admission, serum calcium concentration was 2.95 mmol/l (normal 2.20–2.70 mmol/l), ionised calcium 1.54 mmol/l (normal 1.15–1.35 mmol/l); phosphate 0.90 mmol/l (normal 0.80–1.50 mmol/l), and PTH 5.3 μg/l (normal 0.22–0.50 μg/l). Serum creatinine concentration was 177 μmol/l (normal 60–130 μmol/l) and serum carbamide level was 10.3 mmol/l (normal 2.5–7.5 mmol/l).

Ultrasound disclosed a 2 cm × 1 cm × 1 cm echo-poor nodule posterior to the lower pole of the right thyroid lobe. Ultrasonically guided fine-needle aspiration biopsy was performed, revealing a high concentration of PTH in the aspirate. Cytological examination for parathyroid cells was inconclusive. Surecut biopsy was not carried out.

The parathyroid tumour was treated percutaneously with injection of 0.5 ml and 0.7 ml of ethanol without any decrease in the serum concentrations of ionised calcium and PTH (Fig 2). The patient underwent surgical exploration and three hyperplastic parathyroid tumours were found, of which two had been missed by ultrasound. During and following treatment no complications were observed. Post-operatively, serum concentrations of ionised calcium and PTH decreased.

### *Case 2*

A 63-year-old woman presented with hypercalcaemia and back pain. Since 1980 she had been treated by haemodialysis for renal failure secondary to chronic glomerulonephritis, diagnosed in 1973. Since childhood she had suffered from bronchial asthma and she now exhibited severely reduced cardiopulmonary function.

For 3 years she had had biochemical evidence of HPT with constantly elevated serum concentrations of calcium and PTH.

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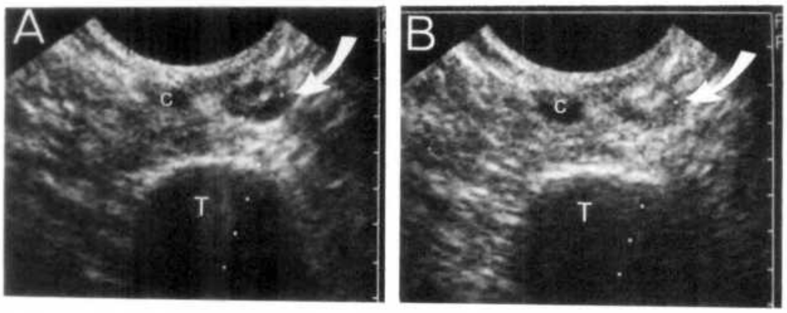

FIG. 1. *Case 1.*

Oblique scans of the neck just caudal to the lower pole of the right thyroid lobe, showing a parathyroid tumour (arrow). An electronic puncture line is seen passing through the parathyroid tumour. "c" indicates the common carotid artery, "T" the trachea. In (A) the needle-tip echo is seen inside the parathyroid tumour. In (B) the parathyroid tumour has become echogenic following alcohol injection.

On admission, serum calcium concentration was 2.80 mmol/l; ionised calcium 1.41 mmol/l; phosphate 0.92 mmol/l; and PTH 12.2 μg/l. Serum concentration of creatinine was 1098 μmol/l and that of carbamide 31.5 mmol/l.

Ultrasound revealed a 1.4 cm × 0.8 cm × 0.6 cm echo-poor nodule located posterior to the lower pole of the right thyroid lobe. Ultrasonically guided fine-needle aspiration biopsy revealed parathyroid cells and a high concentration of PTH in the aspirate. A Surecut biopsy revealed parathyroid tissue.

Because of the surgical risk associated with cardiopulmonary disease, the parathyroid tumour was treated percutaneously with alcohol injection. Initially 0.7 ml of ethanol was injected without beneficial effect. The treatment was repeated 1 month later using 1.0 ml of ethanol. Following this

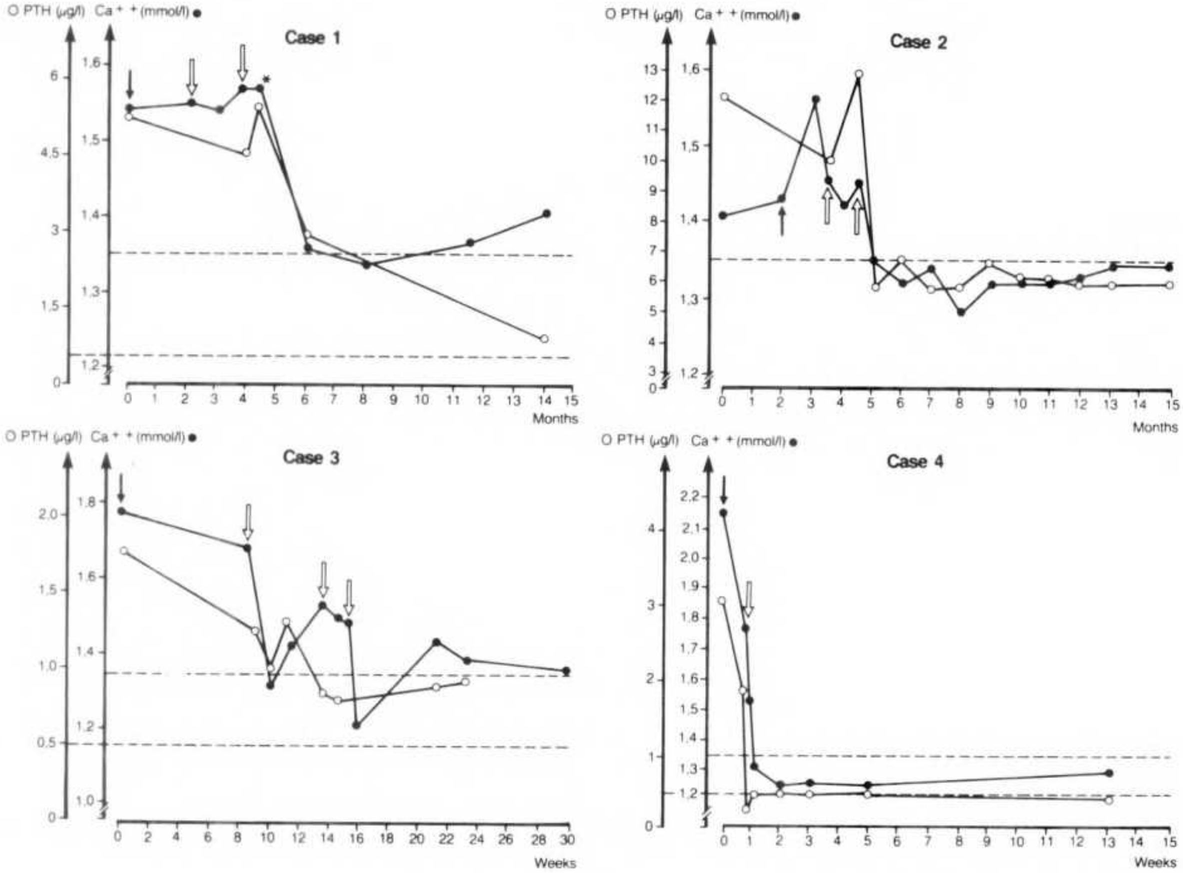

FIG. 2.

Serum concentrations of PTH and ionised calcium following alcohol treatment: serum PTH (○); serum ionised calcium (●); fine-needle biopsy (→); alcohol injection (⇒); and surgery (✱). The dotted lines indicate upper normal limits for serum concentrations of PTH and ionised calcium.

the serum concentrations of PTH and ionised calcium returned to normal and have remained so for a follow-up of 10 months (Fig. 2). No complications were observed during or following the treatment.

*Case 3*

A 64-year-old woman with chronic cor pulmonale was initially admitted for treatment of a toxic thyroid nodule with radioactive iodine. After the radioiodine treatment the serum calcium level remained high in spite of normal thyroid function. Primary HPT was suspected and biochemically verified.

On admission, the serum concentration of calcium was 3.20 mmol/l; ionised calcium 1.79 mmol/l; phosphate 0.83 mmol/l, and PTH 1.7 μg/l. Serum creatinine concentration was normal.

Ultrasonic examination disclosed a 1 cm × 1 cm × 1 cm echo-poor nodule posterior to the lower pole of the left thyroid lobe. Fine-needle aspiration biopsy revealed parathyroid cells and a high concentration of PTH in the aspirate. Surecut biopsy was inconclusive.

Because of the high surgical risk associated with cardiopulmonary disease, the parathyroid tumour was treated three times by percutaneous injection of alcohol. Injections of 1.0, 0.6 and 0.6 ml, respectively, were given (Fig. 2). Following the alcohol treatment, serum concentrations of ionised calcium and PTH decreased. No complications were observed during or following the treatment.

After a follow-up of 5 months the patient died from respiratory insufficiency.

*Case 4*

A 68-year-old man presented with fatigue, muscle weakness, abdominal symptoms, back pain, polyuria and polydipsia. One year previously he had had a Stokes-Adams attack and atrial fibrillation, bundle branch block and heart block of third degree were diagnosed.

On admission, the serum calcium concentration was 3.50 mmol/l; ionised calcium 2.16 mmol/l, phosphate 0.81 mmol/l; PTH 3.0 μg/l, and creatinine 148 μmol/l. A radiograph of the chest was normal.

Ultrasound disclosed a 2 cm × 1 cm × 1 cm echo-poor nodule located posterior to the lower pole of the left thyroid lobe. Fine-needle aspiration biopsy revealed parathyroid cells and a high concentration of PTH in the aspirate. Surecut biopsy revealed parathyroid tissue.

Because of severe hypercalcaemia and the patient's poor clinical condition, treatment had to be undertaken urgently. As the patient refused admission, it was decided to treat him as an outpatient with percutaneous alcohol injection.

One millilitre of ethanol was injected and following this the serum concentrations of ionised calcium and PTH fell and were normal for a follow-up of 3 months (Fig. 2). Two days after the alcohol treatment the patient returned to work as his symptoms had disappeared. No complications were observed during or following the treatment.

## DISCUSSION

The ability to place needles precisely in parathyroid tumours under ultrasonic guidance provides a new possibility of percutaneous treatment. In principle, a wide variety of agents can be introduced through the needle into the tumour. Alcohol has been reported to provide permanent tissue ablation and vascular occlusion (Uflacker et al, 1986).

In three of four patients the desired change in biochemical parameters was observed following alcohol injection. In two of these patients (Cases 2 and 4) normocalcaemia was achieved for a follow-up of 10 months and 3 months, respectively. In the third patient (Case 3) a decrease in the serum level of ionised calcium was observed for the follow-up period of 5 months.

The amount of ethanol given was an arbitrary dose not exceeding 1.0 ml per injection. From several peroperative fine-needle punctures and injections of up to 1.0 ml saline into parathyroid tumours, we did not observe any escape of fluid from the tumours via the needle track. Theoretically, damage to the recurrent laryngeal nerve is a possibility. However, using small amounts of ethanol and precise placement of the needle tip in the centre of the parathyroid tumour, we presume that the risk is minimal.

In two patients (Cases 3 and 4) a decrease in serum levels of PTH and ionised calcium was observed following fine-needle biopsies for tissue diagnosis. According to previous studies (Doppman et al, 1983; Solbiati et al, 1985) intraglandular haemorrhage and necrotic changes have been observed in operative specimens of parathyroid tumours that have undergone pre-operative fine-needle aspiration biopsies, therefore concurrent causes of parathyroid tissue ablation may be present.

The patients in this preliminary study were primarily selected for alcohol treatment because of the high surgical risk or the patient refusing surgery. Today approximately 70–90% of parathyroid adenomas can be detected by ultrasonic scanning (Butch et al, 1985) and their true nature verified by means of ultrasonically guided fine-needle biopsies. In future, these adenomas may be treated percutaneously, *e.g.* with injection of alcohol, providing that larger, controlled clinical series show persistent decrease in serum calcium concentration and that damage to the recurrent laryngeal nerve proves to be either absent or very rare. Non-detectable parathyroid adenomas and diffuse hyperplasia will probably still require surgery. In cases where more than one parathyroid tumour is present and only one is ultrasonically detected the treatment will obviously be insufficient. However, the technique is not stressful for the patient and the operative field is unaffected for subsequent surgery.

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1987, *The British Journal of Radiology*, *60*, 671–675 JULY 1987

# Comparative trial of Hexabrix (320 mg iodine/ml), iohexol (300 mg iodine/ml) and Iopamiron (300 mg iodine/ml) in cerebral and spinal angiography: a preliminary report

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(*Received February 1986 and in final form November 1986*)

ABSTRACT

A comparison has been carried out of results of cerebral and spinal-cord angiography with two non-ionic contrast media, iohexol and Iopamiron, and a low-osmolality contrast medium, Hexabrix. A comparative study of iohexol, Hexabrix, and Iopamiron was carried out in a first group of 41 patients, and Hexabrix was compared with Iopamiron in a second group of 56 Evaluation criteria included local and general safety, as well as quality of angioscopy and angiography. In the first group of patients there were no significant differences in safety between the three agents On the other hand, quality of visualisation during angioscopy with Hexabrix was clearly better In the second group, safety and quality of the radiographic images were identical; however, once again, quality of angioscopy was better with Hexabrix than with Iopamiron We conclude that Hexabrix appears to be the best opacifying agent currently available for cerebral and spinal-cord angiography. While results with Iopamiron were quite similar, the latter agent is slightly more expensive.

Due to their high degree of safety, non-ionic opacifying agents are seeing increasing use in angiography (Ahlgren, 1982; Amundsen et al, 1982; Bettmann, 1982; Nakstad et al, 1982; Holtas et al, 1983; Pelz et al, 1984); nevertheless, their utilisation is frequently limited by price. We considered it of interest to compare the two principal non-ionic opacifying agents in current use for cerebral angiography, iohexol and Iopamiron, with a low-osmolality, ionic contrast agent which is slightly less expensive in France, Hexabrix.

The comparison considered both safety (local and general) of the contrast agents and quality of imaging, both for fluoroscopy, important in superselective angiography, and for angiographic films.

## MATERIAL AND METHODS

The first phase included 41 patients: 15 receiving iohexol (300 mg iodine/ml; Omnipaque 300, Winthrop), nine receiving Hexabrix (320 mg iodine/ml; sodium and meglumine ioxaglate, Guerbet), and 17 receiving Iopamiron (300 mg iodine/ml; iopamidol, Schering).

A second study compared only Hexabrix and Iopamiron in 56 patients. Indeed, during the course of the comparative study, iohexol was eliminated by the three vascular radiologists carrying out the studies (P. Lasjaunias; L. Lopez-Ibor; P. H. Halimi) since fluoroscopic imaging was of poor quality, rendering proper localisation difficult or impossible in spinal-cord angiography. Thus, 29 patients received Hexabrix and 27 received Iopamiron.

The study considered cerebral or spinal-cord angiography carried out for diagnostic and therapeutic purposes in various circumstances (tumours, arterio-venous malformations, strokes, pre-surgical identification of spinal vascular structures, etc.).

There were no exclusion criteria. Examinations were performed under either local or general anaesthesia.

The agent used was determined each day by a random draw. The same medium was used in all examinations carried out on a given day (so as not to have to change the injector syringe and discard the remaining contrast agent). For each examination, a general questionnaire was filled in, noting pre-medication, type of anaesthesia (local or general), dose of contrast medium, concurrent medication and total duration of the examination. For each injection of contrast medium, an information form was filled in by the anaesthetist, indicating dose injected, pulse rate, systemic blood pressure before and after injection, occurrence of arterial spasm, and any sign of intolerance: pain, heat, nausea, vomiting or skin eruptions. Of course, certain of these signs could be evaluated only when the examination was performed under local anaesthesia.

During the 24 h following the examination, any sign of intolerance (nausea, skin eruption, vomiting) and diuresis was noted. The radiological quality of results was indicated by the radiologist who had performed the angiography.

### *Randomisation*

On each day of the study, all patients received one of the three (or two) agents, with allocation on the basis of a randomisation table, itself established from a random-numbers table The test was carried out double-blind, both the patient and the physician being unaware which contrast medium was injected.

### *Evaluation criteria*

The primary criterion was safety local (pain at the injection site, arterial spasm), and systemic (sensation of

TABLE I

COMPARISON OF THE THREE AGENTS IN CEREBRAL AND SPINAL CORD ANGIOGRAPHY (41 PATIENTS)

| | Iohexol<br>(15 patients) | Hexabrix<br>(nine patients) | Iopamiron<br>(17 patients) | |
|---|---|---|---|---|
| Anaesthesia: local | 7% (1) | 22% (2) | 18% (3) | NS |
| general | 93% (14) | 78% (7) | 82% (14) | NS |
| Duration of examination (min) | 75.0 (9) | 73.8 (8) | 91.8 (14) | NS |
| Number of injections | 4.7 | 4.4 | 5.9 | NS |
| Total quantity (ml)/patient | 55.9 | 45.3 | 51.7 | NS |
| Safety over 24 h | | | | |
| Nausea | 8% (1/13) | 11% (1/9) | 31% (5/16) | NS |
| Vomiting | 8% (1/13) | 11% (1/9) | 0 | NS |
| Skin eruption | 0 | 0 | 0 | |
| Polyuria | 43% (6/14) | 0 | 13% (2/16) | SS |
| Headache | 8% (1/13) | 0 | 25% (4/16) | NS |
| Quality of the examination | | | | |
| Angioscopy poor | 7% (1) | 0 | 0 | |
| fair | 57% (8) | 11% (1) | 63% (10) | NS |
| good | 36% (5) | 89% (8) | 38% (6) | SS |
| Films: poor | 36% (5) | 0 | 25% (4) | NS |
| satisfactory | 64% (9) | 100% (9) | 75% (12) | SS |

Number of patients is shown in parentheses NS = not significant, SS = statistically significant ($p < 0.05$)

heat, nausea, vomiting, skin eruptions, changes in the diuresis, pulse rate or blood pressure).

Quality of contrast during the initial arterioscopic procedure was considered to constitute a valid evaluation criterion, since proper visualisation of the catheterised vascular network and the territory supplied is essential for rapid and successful hyperselective angiography

## RESULTS

For comparison of iohexol, Hexabrix and Iopamiron, see Tables I and II. For comparison of Hexabrix and Iopamiron, see Tables III and IV.

Patient groups were balanced in terms of sex, height and body weight Comparing iohexol, Hexabrix and Iopamiron in terms of safety over 24 h (Table I), no statistically significant differences were observed, except for hyperdiuresis seen in 43% of cases with iohexol, 13% (two of 16) with Iopamiron and none with Hexabrix. In view of the small number of studies performed under local anaesthesia in the first patient group (six cases), subjective symptoms upon injection (pain, heat, nausea, vomiting, headache) are not shown in Table III, and only haemodynamic changes (pulse rate, blood pressure, arterial spasm) are noted. There were no significant differences between the three agents for these criteria.

In the second patient group (comparative study of Hexabrix and Iopamiron; Tables III and IV) there were no significant differences in terms of side-effects or vascular spasm Similarly, the sensation of heat upon injection was reported by two of nine patients in the

TABLE II

HAEMODYNAMIC SAFETY OF INJECTION OF THE THREE CONTRAST AGENTS (207 INJECTIONS)

| | Iohexol<br>(70 injections, 34%) | Hexabrix<br>(40 injections, 19%) | Iopamiron<br>(97 injections, 47%) |
|---|---|---|---|
| Dose (ml) (mean/injection) | 11.5 (69) | 10.2 (40) | 9.2 (94) |
| Pulse rate (per min) before injection | 67.8 (70) | 72.9 (40) | 70.4 (96) |
| Pulse rate (per min) (after – before) | −0.4 (69) | −1.1 (39) | +0.4 (96) |
| Blood pressure before injection (cm Hg) (max.) | 10.9 (70) | 10.7 (40) | 10.2 (97) |
| Blood pressure (cm Hg) (after – before) | +0.2 (69) | −0.03 (39) | +0.2 (97) |
| Arterial spasm | 13% (8/63) | 3% (1/29) | 6% (4/69) |

The number of injections is shown in parentheses

TABLE III

Comparison of Hexabrix and Iopamiron in cerebral and spinal-cord angiography (56 patients)

| | Hexabrix (29 patients) | Iopamiron (27 patients) | |
|---|---|---|---|
| Local anaesthesia | 24% (7) | 19% (5) | NS |
| General anaesthesia | 76% (22) | 81% (22) | NS |
| Duration of examination | 71.4±32.6 | 83 3±34 0 | NS |
| Number of injections | 4.1±1.7 | 4.9±2 5 | NS |
| Frequency: 1 injection | 1 | – | |
| 2 injections | 1 | 2 | |
| 3 injections | 9 | 8 | |
| 4 injections | 10 | 5 | |
| 5 injections | 6 | 4 | |
| 6 injections | – | 2 | |
| 7 injections | – | 3 | |
| 9 injections | 2 | 1 | |
| 10 injections | – | 1 | |
| 12 injections | – | 1 | |
| Mean total quantity (ml) | 40.2 | 43.5 | |
| Safety over 24 h | | | |
| Nausea | 3% (1) | 23% (6) | NS |
| Vomiting | 7% (2) | 0 | NS |
| Eruption | 3% (1) | 0 | NS |
| Polyuria | 3% (1) | 19% (5) | NS |
| Headache | 0 | 15% (4) | NS |
| At least one of these signs | 14% (4) | 33% (9) | NS |
| Quality of examination | | | |
| Angioscopy: poor | 0 | 0 | |
| fair | 34% (10) | 62% (16) | SS |
| good | 66% (19) | 38% (10) | SS |
| Films: poor | 7% (2) | 15% (4) | NS |
| satisfactory | 93% (24) | 85% (22) | NS |

The number of patients is shown in parentheses. NS = not significant, SS = statistically significant ($p$ 0.05)

Hexabrix group. The 24 h tolerance of Iopamiron appeared to be slightly less good than that of Hexabrix (respectively 23% and 3% for nausea, 19% and 3% for hyperdiuresis); however, these differences were not statistically significant.

In terms of quality of arterioscopic imaging, comparison of the three agents in the first patient group (Table I) showed 89% good results with Hexabrix, compared with 36% and 38% respectively for iohexol and Iopamiron. Comparison of results for Hexabrix and Iopamiron (Table III) showed 66% good results with the former agent and 32% with the latter; this difference was statistically significant. On the other hand, the latter two agents yielded similar results in terms of the graphic image (93% of films satisfactory with Hexabrix, vs 85% with Iopamiron).

## Discussion

From the results of this study, we cannot consider that non-ionic contrast agents constitute a major improvement in cerebral or spinal angiography in comparison with the weakly hyperosmolar ionic agents such as Hexabrix. There are no significant differences in most parameters of safety between the three agents and hyperdiuresis is not observed with Hexabrix. It has been established (Evill & Benness, 1978; Brennan et al, 1982) that the reduced effect of Hexabrix on osmotic diuresis results from the decreased urinary solute excretion due to the higher sodium reabsorption by the renal tubules from the sodium salts.

It has been also suggested (Ahlgren, 1982) that hyperdiuresis was related to vascular effects on the brain. Transient cerebral ischaemia is caused by the sludge phenomenon and is magnified by hydrodynamic changes and arterial spasm. Recently, du Boulay and Wallis (1986) showed that, in baboons, cerebral vasoconstriction caused by Hexabrix had largely disappeared after 20 min, whereas iohexol caused more persistent vasoconstriction. Wilcox et al (1986) observed neurological reactions in rabbits with all intracarotid injections of a non-ionic monomer

TABLE IV

COMPARISON OF INJECTIONS OF HEXABRIX AND IOPAMIRON (246 INJECTIONS)

| | Hexabrix (118 injections, 48%) | Iopamiron (128 injections, 52%) | |
|---|---|---|---|
| Dose of the contrast medium (mean/injection) | 9.8±3 3 | 9 4±4 4 | |
| Injection site | | | |
| Vertebral | 25 | 23 | |
| Carotid | 55 | 56 | |
| Medullary | 14 | 16 | |
| Meningeal | 2 | 8 | |
| Pharyngeal | 3 | 1 | |
| Maxillary | 7 | 7 | |
| Occipital | 2 | 2 | |
| Thyroid | 1 | 3 | |
| Facial | 2 | 6 | |
| Other | 4 | 6 | |
| Pulse rate after–before injection (per min) | −0 9±3.2 | +0.4±5.3 | NS |
| Blood pressure (cm Hg) after–before injection | 0.07 0 57 | 0 16 0 92 | NS |
| Arterial spasm | 2% (2/99) | 4% (4/99) | NS |
| Pain | 5% (2/41) | 0 (0/32) | NS |
| Heat | 10% (4/41) | 3% (1/30) | NS |
| Nausea | 0 | 0 | |
| Vomiting | 0 | 1% (1) | NS |
| Eruption | 0 | 1% (1) | NS |
| Headache | 0 | 0 | |

The number of injections is shown in parentheses, NS = not significant

(iopromide) and a non-ionic dimer (iotrol). No reactions were observed with an ionic monomer (meglumine iothalamate).

The quality of real-time angioscopic imaging appears to be of particular importance in hyperselective angiography; indeed, excellent contrast quality is required in spinal angiography for identification of radicular vessels supplying the cord (avoiding wasted injections), as well as for therapeutic angiography. The higher iodine titre of Hexabrix (320 mg/ml versus 300 mg/ml for the other two media) and its slightly higher viscosity by comparison with non-ionic media (Sage, 1983) (Table V) are two factors which do not appear to be sufficient to explain the excellent quality of imaging it provides. This difference might possibly be due to the arterial constriction that occurs with non-ionic contrast media. In contrast, low-osmolar or ionic contrast media cause vasodilatation. In a recent *in-vitro* study Donadieu et al (1987) demonstrate a significant decrease in blood filtrability by sludge effect with iohexol and Iopamiron, while filtrability with Hexabrix was not modified.

TABLE V

PHYSICOCHEMICAL PROPERTIES

| | Osmolality (mOsmol/kg) | Viscosity (cps) at 37°C |
|---|---|---|
| Omnipaque (iohexol) | | |
| Omnipaque 240 | 500 | 3 3 |
| Omnipaque 300 | 690 | 6.1 |
| Omnipaque 350 | 880 | 10 6 |
| Iopamiron (iopamidol) | | |
| Iopamiron 200 | 413 | 2.0 |
| Iopamiron 300 | 616 | 4.5 |
| Iopamiron 370 | 800 | 9.5 |
| Hexabrix (ioxaglate) | | |
| Hexabrix 320 | 600 | 7 5 |

In contrast with certain published studies (Nakstad et al, 1982; Holtas et al, 1983; Pelz et al, 1984; Valk et al, 1984), the safety of iohexol seems slightly less good and quality of imaging relatively poor. Comparing Iopamiron with Hexabrix, the latter showed a slight advantage in terms of angioscopic imaging. Safety, both immediate and over the first 24 h, was excellent with both agents, with no significant differences.

In conclusion, Hexabrix currently appears to be the best contrast medium for cerebral and spinal angiography, in terms both of quality of angioscopic and angiographic imaging, and of safety; results with Iopamiron are very similar

ACKNOWLEDGMENT

This study was carried out with the assistance of the INSERM Research Foundation, Contract No. 130010

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# Book reviews

*Dosimetry and Clinical Uses of Afterloading Systems* Ed. by A R Alderson, pp 88, 1986 (Institute of Physical Sciences in Medicine, London), £12 00.
ISBN 0–904181–40–5

This book reports the proceedings of a meeting of the Institute of Physical Sciences in Medicine held at St Bartholomew's Hospital in May 1985. It is, therefore, a useful guide to the different techniques currently available for the afterloading of sealed radioactive sources for intracavitary radiotherapy

The first two chapters examine the radiobiology and the techniques for high-dose-rate afterloading High dose rate in this context is about 3 Gy $\mathrm{min}^{-1}$ to Point A Chapter 1 highlights some of the anomalies in current statements of dose and Chapter 2 outlines the changes in the pattern of work which result from adopting this technique. Both chapters conclude that large departments with a significant demand for intracavitary radiotherapy should adopt high-dose-rate afterloading, while smaller departments should content themselves with manual afterloading

Two chapters are devoted to the Amersham manual afterloading technique. The first of these is a critical account of the techniques adopted to calibrate the source activity and the calculation of dose tables. While being very theoretical and quoting figures to an order of magnitude greater than clinical accuracy demands, the worked example and the dose tables are valuable We are coming to accept that this area of dosimetry commands a confusion of units, both old and new, and this and other chapters in the book confirm this trend. The contributor, after a page of calculations in the old units, states boldly, "In future all gamma radiation sources will be specified in SI units" Let us hope so The contribution from the Royal Free Hospital, reporting their experience of using this manual afterloading system, is valuable in that it not only describes the technique in some detail, but goes on to outline the problems of nursing these patients on the ward with the attendant radiation hazard and the planning of the post-caesium X-ray treatment

The outline of the Curietron afterloading technique describes the equipment and the design of the source trains. It then goes on in some detail about the commissioning tests on the source trains and the measurements that can be made to assess the uniformity, or otherwise, of source activity It concludes with some data on the radiation field around the patient's bed and a brief account of the machine faults encountered over the years The oscillating uterine source of the Buchler system at the Hammersmith Hospital concludes the survey of afterloading equipment. The paper deals with the dosimetric checks and the densitometric checks made of the isodose data for this moving source and concludes with some analysis of the procedure itself and of the results to date

Another contribution discusses the dosimetry of afterloaded flexible sources of iridium wire following the Paris system and a system of optimisation based on the fast computation of dose using "permissible" approximations The last chapter is devoted to the stereotactic insertion of iodine-125 sources into brain tumours The properties of these sources, the procedures followed and the encouraging clinical results from the first 118 implants are discussed.

The major shortcoming of the book was not so apparent at the meeting itself. There is no reference to what must be the most widely adopted remote afterloading technique for gynaecological treatment, namely the Selectron. The book itself would have been a more complete guide to the dosimetry and clinical uses of afterloading systems had this been included. The reader has to be content with two related contributions, the first based on the computed tomography scanning of the patients treated at the Christie Hospital, Manchester. These scans, together with detailed dose computations, have resulted in one in four insertions being modified in one way or another—either a modification of the treatment time or the repositioning of the sources to reduce the dose to critical tissues, *e g* the rectum Finally, there is a brief outline of the technique for the treatment of the oesophagus using the Selectron.

Accepting this quite serious omission, the book is to be recommended as a guide to afterloading. The reader will do well not to confine himself to the chapters devoted to any one technique

C. K. BOMFORD

*SPECT Single-Photon Emission Computed Tomography A Primer.* By R. J. English and S. E Brown, pp xv + 148, 1986 (Society of Nuclear Medicine, New York), $17.00
ISBN 0–932004–24–5

Single-photon emission computed tomography (SPECT) systems are now widely used for tomography in nuclear medicine This book is a primer published by the American society of Nuclear Medicine (SNM) aimed at technicians. It is intended to be a rather elementary and very practical introduction to the subject, to provide information on running such a system, and to give guidance in quality assurance. It certainly fills a need The only comparable book is probably the Institute of Physical Science in Medicine handbook (IPSM 44) *An Introduction to Emission Computerized Tomography*, which is aimed more at physicists. The SNM book describes image acquisition, reconstruction and processing in SPECT, and has a very good chapter on quality assurance and another rather limited chapter on clinical applications There is an excellent glossary, a reasonable reading list and a good index. Study questions (and answers) are given for each chapter

It is certainly to be recommended as an excellent introduction—but . . . The "but" is common to many books of this type; there are quite a lot of errors, misunderstandings and omissions Only rotating gamma-camera systems have been considered It is a pity that the images illustrating the importance of quality control are of such poor quality themselves, and are not of the commonly used Jaszczak phantom. The descriptions of attenuation correction and quantification are very poor Some of the answers to the study questions are debatable It is a pity that only the (probably) inferior method of centre of rotation correction has been described And so on However, it is a short book of only 147 pages and, apart from these niggles, is welcomed as a good practical introduction to the field.

A TODD-POKROPEK

1987, *The British Journal of Radiology*, 60, 677–680 JULY 1987

# The prediction of the relative toxicities of radium 224 and of radium 226 in the bones of mice using Monte Carlo techniques

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*(Received August 1986 and in revised form January 1987)*

ABSTRACT

Toxicity studies using rodents have shown that the long-lived radium isotope radium 226 is about six times less toxic per unit of absorbed radiation dose to the skeleton than the short-lived isotope radium 224 with respect to the production of osteosarcoma This difference in toxicity has been attributed to differences in the distribution of these isotopes It has been suggested that $^{224}$Ra is more toxic than $^{226}$Ra because it decays on bone surfaces rather than within the volume of the bone mineral However, in rodents many bone structures are small compared with the track length of the $\alpha$ particles and this explanation may be inadequate to explain the magnitude of the observed effect Consequently, Monte Carlo calculations have been made to test the validity of the distribution-difference hypothesis. The results indicate that, for bone structures the size of those in mice, less than half of the observed difference in toxicity can be explained by considerations of the distribution of these radionuclides with respect to bone surfaces Instead, it is suggested that the greater irradiation of trabecular than of cortical bone that is a characteristic of $^{224}$Ra is responsible for its enhanced toxicity.

Bone sarcoma is the most common late effect following the intake of $\alpha$-particle-emitting, bone-seeking radionuclides by man (Vaughan, 1973). The likely magnitude of this effect has been largely determined by reference to human toxicity data, which exist only for the short-lived isotope radium 224 ($t_{\frac{1}{2}} = 3.64$ days) and for the long-lived isotope radium 226 ($t_{\frac{1}{2}} = 1600$ years). Of these, $^{224}$Ra is the more toxic. It follows that studies of the metabolism, dosimetry and toxicity of radium isotopes are potentially of great significance in radiological protection. For this reason many such studies have been undertaken in laboratory animals.

Toxicity studies using these radionuclides in mice have shown that, as in man, $^{224}$Ra induces significantly more bone sarcomas than $^{226}$Ra per unit of average dose-equivalent to the skeleton. For example, the results of the studies of Kofránek et al (1978) suggested that $^{224}$Ra is about three to five times more efficient in producing tumours than $^{226}$Ra, and Müller et al (1983) reported that this factor may be as high as seven.

The difference in the toxicity of these isotopes is most commonly attributed to differences in the spatial distribution of the decay events of the radionuclides in the skeleton. Radium 224 is taken to decay at the sites of radium deposition on bone surfaces adjacent to the radiosensitive bone surface-lining cells. This assumption is a consequence of its short half-life, which gives little time for radionuclide redistribution. In contrast, most of the long-lived $^{226}$Ra isotope becomes redistributed, by the processes of bone turnover and heterionic exchange, throughout the volume of the bone mineral prior to decaying. Consequently, much more of the decay energy of $^{226}$Ra is harmlessly attenuated by the mass of bone mineral.

However, while this explanation has been considered adequate to explain the relative toxicities of radium isotopes in large animals and in man, it may not explain the magnitude of the difference of this effect in mice. This is because of the small size of mouse bones and their fine structure relative to the track length of the radium $\alpha$ particles. This could result in a significant dilution of the difference between the irradiation of bone surfaces by a bone surface-distributed and by a similarly radioactive bone volume-distributed radionuclide, due to cross-irradiation.

In order to examine the influence of skeletal dimensions on the size of the bone-volume/bone-surface effect the following Monte Carlo calculations were made. The results of these calculations suggest that less than half of the observed difference between the toxicity of $^{224}$Ra and $^{226}$Ra in mice can be explained by the decay distribution patterns of these isotopes relative to bone surfaces.

## CALCULATIONS

For the calculations, $^{224}$Ra was assumed to decay either with the emission of a single $\alpha$ particle of energy 5.66 MeV or with the emission of four $\alpha$ particles of 5.66, 6.28, 6.78 and 7.82 MeV respectively. Radium 226 was assumed to decay either with the emission of a single 4.77 MeV $\alpha$ particle or with the emission of five particles with energies of 4.77, 5 48, 6.00, 7.68 and 5.31 MeV respectively. In order to account for the diminution of the radiation dose to bone surfaces caused by the migration of radon from the skeleton, the number of single decays assumed for the calculations were 50 per 100 for $^{224}$Ra on bone surfaces

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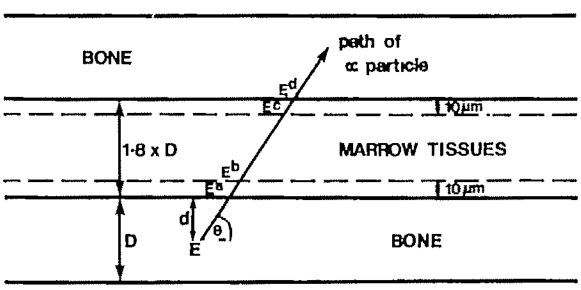

FIG. 1.

Diagram outlining the bone model used for the calculations. For volume-distributed radium the solid angle ($\theta$) and the depth of burial of the disintegrating radium atom below the bone surface ($d$) in bone of width $D$ are allocated randomly. For surface-deposited radium the value of $D$ is taken to be zero The residual energy of the α particles at each interface ($E_a$, $E_b$, $E_c$ ) was calculated and used to determine the fraction of the total α energy deposited in the bone surface layer of the bone marrow (dotted lines) and in the total bone-marrow tissues

(Humphreys et al, 1984), 0 per 100 for $^{224}$Ra in the bone volume, and 15 per 100 for $^{226}$Ra (Mays et al, 1963). The precise values for these fractions, which were derived experimentally, were not critical for the calculations. Where appropriate, all daughter decays were assumed to originate at the site of the decay of the parent radionuclide. The range ($R$) in μm of the α particles of energy ($E$) in the bone mineral (μm) was determined using a six-degree polynomial (personal communication, A. C. James, National Radiological Protection Board, Chilton, Didcot, Oxon, UK):

$$R = 0.1764+4.7827E-0.1922E^2+0.4114E^3-0.1083E^4 +0.0138E^5-6.4478\mathrm{e}^{-4}E^6$$

The residual energies of α particles after travelling a given distance in bone were calculated using an eight-degree polynomial which expresses α energy ($E$) as a function of range ($R$):

$$E = -4.2003\mathrm{e}^{-2}+1.7991\mathrm{e}^{-1}R+8.6544\mathrm{e}^{-3}R^2- 1.0842\mathrm{e}^{-3}R^3+4.9426\mathrm{e}^{-5}R^4-1.1852\mathrm{e}^{-6}R^5+ 1.5725\mathrm{e}^{-8}R^6-1.0904\mathrm{e}^{-10}R^7+3.0827\mathrm{e}^{-13}R^8$$

For the calculations, α particles were assumed to travel 1.55 times as far in the bone marrow as in the mineralised bone matrix.

The bone model used for the calculations is given in Fig 1. The bone was considered to consist of a stack of parallel plates separated from each other by bone marrow tissues. An alternative model based on cavities of defined widths within solid bone was not used. However, calculations made using such a model by Montelius and Burlin (1984), for the bone volume-seeking radionuclide $^{226}$Ra and for the bone surface-seeker plutonium 239, suggest that, for bone cavities of a similar size to those found in man, both the cavity model and the parallel-plate model produce similar results. The width of each plate was varied between arbitrary limits of 10 μm and 250 μm. The width of the bone marrow spaces was taken to be 1.8 times the appropriate bone width. This ratio was used because it corresponds to an average ratio measured in the bones of mice (Table I). However, in some regions of the skeleton, including the shafts of long bones, the width of the marrow spaces will be considerably larger than this average. Radium and daughter disintegrations were assumed to originate either at the surfaces of the bony plates or at a random depth within them. The random depths were produced using a computer-generated random number. The same generator was used to produce the three-dimensional co-ordinates of random solid angles. These solid angles were used to define the trajectory of the α particles (Thorne, 1977). The amounts of α energy deposited in bone marrow tissue and in the regions of this tissue up to 10 μm from the bone surfaces (an arbitary figure commonly used to define the limits of the bone surface layer) were calculated. Calculations were made for 10000 radium disintegrations for each bone width and for $^{224}$Ra distributed either as a bone-surface or as a bone-volume deposit, and for $^{226}$Ra present as a volume deposit. In addition, a calculation was made assuming $^{224}$Ra to be half surface-deposited and half volume-deposited. This latter calculation was made because of the suggestion of Spiess and Mays (1973) and others that this is the most appropriate distribution for practical $^{224}$Ra dosimetry.

TABLE I

MORPHOMETRIC PARAMETERS MEASURED FOR THE BONES OF YOUNG ADULT MICE

| Sample | Mean chord length (μm) | | From s · v ratio (μm) |
|---|---|---|---|
| | Bone | Bone marrow | |
| Femur | 83 | 119 | 45.0 |
| Lumbar vertebrae | 72 | 142 | 52.6 |
| Caudal vertebrae | 65 | 72 | 45.4 |
| Ilium | 65 | 178 | 43.4 |
| Mean | 71 | 128 | 46.6 |

Green, D., (personal communication), MRC Radiobiology Unit, Harwell, Didcot, Oxon OX11 0RQ, UK.

RESULTS AND CONCLUSIONS

The fraction of the total skeletal radium α decay energy absorbed in the 10 μm-thick bone surface layers for different bone widths is given in Fig. 2. The corresponding fractions calculated for the total bone marrow tissue are given in Fig. 3. These figures include a line corresponding to the fraction for $^{224}$Ra which would be predicted if its six times greater toxicity was due only to the spatial distribution of its α decays. They also show a shaded band which corresponds to

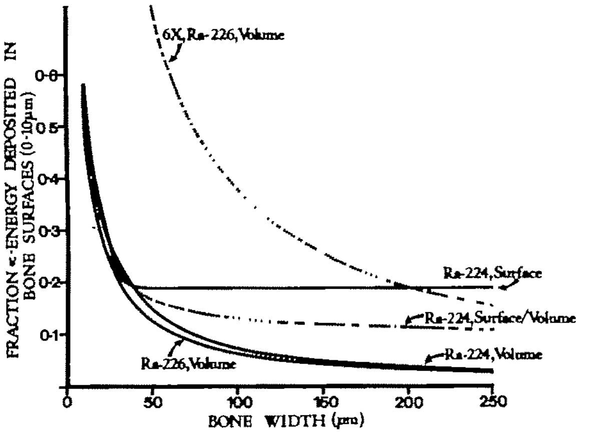

FIG. 2.

Graph showing the calculated values for the fraction of the total α energy emitted by $^{224}$Ra and $^{226}$Ra that is deposited in the 10 μm-thick surface layer of the bone marrow tissue as a function of the assumed average width of the bone structures. Values for $^{226}$Ra present in the bone volume and for $^{224}$Ra present in the bone volume, on bone surfaces and present as a mixed surface and volume deposit, are presented. Also shown is a line corresponding to a fraction six times larger than for that of $^{226}$Ra on bone surfaces and a shaded band corresponding to the range of measured bone chord lengths in mouse bone.

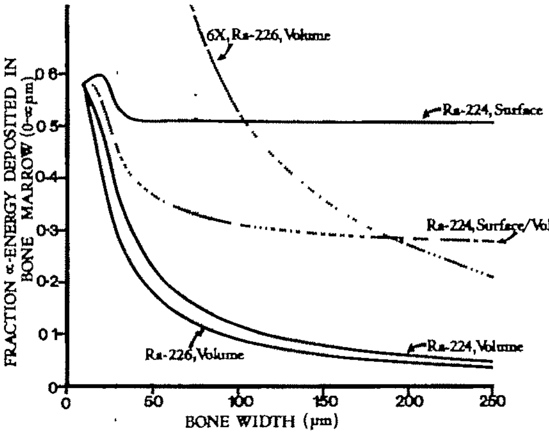

FIG. 3.

Graph similar to Fig 2, for α energy deposited in the total bone marrow.

the range of bone mean chord lengths (Table I), as measured in mice.

It can be seen that the calculated fraction of the α energy deposited in the bone surface layers is little different for the radium isotopes, irrespective of their assumed distribution, up to bone widths equivalent to the range of the α particles in bone, which is about 30 μm. Thereafter, the fraction for $^{224}$Ra deposited on bone surfaces remains constant, whereas the corresponding fractions calculated for volume-distributed radium isotopes continue to fall. The equivalent fractions for the total bone marrow space change in a similar way. However, at small values of bone width the small size of the bone components and the greater volume of bone marrow result in calculated fractions for $^{224}$Ra on bone surfaces which exceed 0.5. Also, whereas the minimum fraction for the total bone marrow for $^{224}$Ra deposited on bone surfaces is 0.5, as is predicted from geometric considerations, that calculated for the bone surface layer is approximately 0.2.

The results show that, for bone widths ranging from 65 μm to 83 μm, corresponding to the measured mean chord lengths in the mineralised bone of mice, the calculated fraction of the total α energy deposited in the bone surface layer for $^{224}$Ra on surfaces is about twice the equivalent fraction for volume-distributed $^{226}$Ra. Provided that the radiation-sensitive, bone sarcoma-producing cells are found close to bone surfaces this value is approximately three times lower than that required to explain the enhanced toxicity of $^{224}$Ra in mice However, the true discrepancy between the observed and predicted toxicities is likely to be larger than three. This is for two main reasons. Firstly, the mouse bone mean chord lengths are larger than the average width of the structures within the bones. For example, if 47 μm, derived from the measured surface-to-volume ratio of the mouse bones, is used as a measure of approximate bone width (Table I) then the fraction of the total α energy absorbed in the bone surface layers necessary to explain the enhanced toxicity of $^{224}$Ra would have to exceed unity slightly. Secondly, the toxicity studies undertaken by Kofránek et al (1978) and by Müller et al (1983) used growing mice. In these animals substantial burial of surface deposits of $^{224}$Ra will have occurred during the period of irradiation of the skeleton. This burial will have decreased the radiation dose to the surface layers of the bone.

Alternatively, if it is assumed that the sensitive target cells are distributed throughout the bone marrow spaces, rather than restricted to bone surfaces, then the discrepancy between the calculated and predicted fractions is smaller, but remains substantial. In this case (Fig. 3), in order to explain the enhanced toxicity of $^{224}$Ra it is necessary to assume that the mouse bone structures are unrealistically massive (about 110 μm wide for a pure surface deposit of $^{224}$Ra or about 190 μm wide—similar in size to the trabeculae of man—for a surface/volume deposit).

In conclusion, in view of the common occurrence of bone sarcomas in the trabeculated regions of rodent bones, the results of the calculations indicate that the reason why $^{224}$Ra is about six times more toxic than $^{226}$Ra in mice is not only that its decay energy is released close to bone surfaces. Indeed, they suggest that an, as yet, undescribed factor may be responsible for a large component of its enhanced toxicity. It is tentatively suggested that this factor may be related to differences in the anatomical location of the surfaces irradiated by the two radium isotopes. If it is assumed that the less metabolically active surfaces of cortical bone are less sensitive to irradiation by α-emitting radionuclides than the equivalent surfaces of trabecular bone then a large part of the greater toxicity of $^{224}$Ra can be explained as follows. Radium 224 may be more toxic than $^{226}$Ra in mice because it is distributed between cortical and trabecular bone, during the period of its irradiation of the skeleton, according to the ratio of trabecular and cortical bone surfaces, which in mice favours trabecular bone, whereas $^{226}$Ra is distributed according to the ratio of bone volumes, which favours cortical bone. If this explanation is valid then it could also explain the observed three times greater toxicity of plutonium than of the trivalent actinides, for equal average radiation doses to the skeleton, in mice and rats (Taylor, 1983; Taylor et al, 1983). This is because the trivalent actinides such as americium deposit on all bone surfaces including the walls of the vascular canals within rodent cortical bone, whereas plutonium deposits preferentially on trabecular surfaces (Priest et al, 1985). It follows from the above that considerable care should be taken when extrapolating the results of relative toxicity studies in rodents to man.

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1987, *The British Journal of Radiology*, *60*, 681–684 JULY 1987

# Valuing the man-sievert in X-ray diagnosis

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(*Received August 1986 and in revised form November 1986*)

ABSTRACT

New advice from the National Radiological Protection Board gives a range of monetary values for the unit collective dose, depending in part on the annual individual dose In this paper the special factors in medical radiodiagnosis are described and a valuation for the man-sievert in this field is suggested The harm to children from ionising radiation may be appreciably larger than in adults, and a different value for children and in obstetrics is suggested

In radiodiagnosis a monetary value of the detriment from exposure to ionising radiation is needed in order to assess the cost effectiveness of methods of protection and for optimisation of methods of radiation protection. The National Radiological Protection Board (NRPB) (1986a) recently offered new advice on this subject, giving a range of monetary values for the man-sievert. This paper looks at the rationale for these valuations and suggests specific values for use in medical diagnosis.

The NRPB's advice is summarised in Fig. 1, which relates the monetary value for the collective effective dose equivalent to the level of the annual individual effective dose-equivalent (abbreviated to dose in the remainder of the paper). There are two components Whatever the level of individual dose, the basic harm of radiation is valued (the $\alpha$ component) At low individual doses this is all, but at higher doses a further component is introduced. This second component, identified by the International Commission on Radiological Protection (ICRP) (1983) as the $\beta$ component, is referred to by them as the "non objective health detriment" and includes factors such as anxiety and aversion to increasing physical risk.

The NRPB agrees that proportionately more resources should be applied to the protection of the individuals at higher risk (*i.e.* higher dose) and this is best achieved by assigning an increased value to collective doses made up of higher individual doses. The values given in Fig. 1 are for the remainder of the 1980s and are intended to apply to all exposures, including medical and natural radiation. Figure 1 also shows typical calculated doses (NRPB, 1986b) for some common radiological examinations. It should be noted, however, that these are not necessarily annual doses. The doses for many radiological examinations (*e.g.* peripheral limb examinations, chest examinations and small dental films) are very small, and despite their relatively higher frequency these examinations make only a small contribution to the collective dose to the population. Most of the collective dose arises from the large-dose examinations, *i.e.* c, d, e and f in Fig. 1.

There are two steps in the assessment of valuing the detriment associated with unit collective dose (1 man-Sv).

(a) What harm does 1 man-Sv cause?
(b) How should this harm be valued?

## HARM CAUSED

### *Cancer production*

Radiation exposure, according to ICRP (1977), gives an estimated fatal cancer risk of 0.0125 $Sv^{-1}$, as an average for both sexes. As a fatal cancer takes 5–30 years to cause death, a proportion of an affected population will die of other causes and in these cases the radiogenic cancer will not appear, so the mortality risk factor can be taken, for a lifetime exposure, as 0.01 $Sv^{-1}$ (ICRP, 1977). In diagnostic radiography, however, exposure is not uniform throughout life. In the United Kingdom in children younger than 10 years the frequency of examination is a third of that for those aged over 60 years (Kendall et al, 1980). In general, the radiation dose for an examination is smaller in children, assuming proper beam collimation for the size of the child. A large proportion of a lifetime's exposure to diagnostic X rays occurs in the patient's last illness when radiogenic cancer is irrelevant. Thus, compared with exposure throughout life, the cancer mortality risk factor for a population exposure from medical diagnosis will be less. We propose that it could reasonably be taken as 0.006 $Sv^{-1}$. Wall (1985) comes to a similar conclusion from medical radionuclide examinations. A further detriment is the causing of a number of curable cancers, approximately equal in number to the lethal cancers—mainly of the skin and thyroid. These are responsible for a treatment cost and also for the worry which they cause.

### *Genetic risk*

The magnitude of the risk to the offspring of a person who is irradiated has been considered (ICRP, 1977), together with the effect of the age and hence child expectancy distribution, in working populations and the general public. In coming to their conclusions the ICRP considers only defects which are expressed in live-born

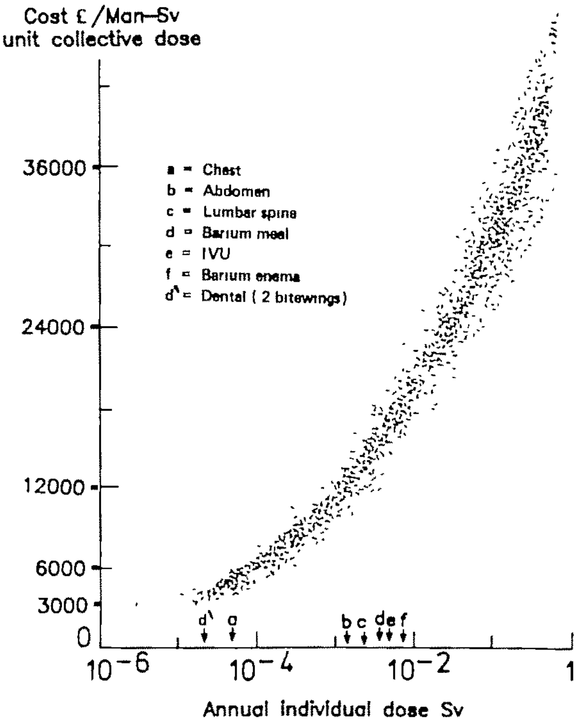

Fig 1

The relationship, suggested by the NRPB (1986a), between annual individual dose and cost of unit collective dose The letters on the abscissa indicate the effective dose-equivalent of some common examinations (Wall, 1986).

children, those leading to stillbirths or abortions being excluded. The risk of a serious genetic defect in the first two generations from the prior irradiation of a parent is 0.01 $Sv^{-1}$. When considering complete populations, a proportion of the exposures (those to patients older than average ages, in each sex, for conception) will have little or no genetic significance On this basis the ICRP indicated that a genetic risk of 0.004 man-$Sv^{-1}$ in the first two generations would apply to uniform irradiation of a general population, with a similar total risk in all subsequent generations. As noted previously, the distribution of dose from diagnostic radiology with age is not uniform, a large proportion being delivered at ages when child expectancy is essentially zero. A larger reduction in the risk factor than that applied to cancers is appropriate for genetic risks since child expectancy falls to zero at lower ages than does life expectancy. A further reduction factor of 0.5 can be estimated from known age/sex and gonad dose distributions for patients in Britain, but this aspect is being investigated further (Wall, 1986). The genetic risk from diagnostic radiology examinations of a general population can therefore be taken to be about 0 001 man-$Sv^{-1}$ in the first two generations and the same total in all subsequent generations, giving a total risk of serious genetic defects from diagnostic radiology of 0 002 man-$Sv^{-1}$.

*Total risk*

For adult patients the harm from 1 man-Sv in radiodiagnosis can be taken as 0 006 of a lethal cancer and 0.002 of a case of serious genetic abnormality in all generations, that is to say 0 008 cases of these radiation injuries from 1 man-Sv.

For obstetric or paediatric work the genetic risk is essentially that from prior irradiation of a parent, *i.e.* about 0.01 man-$Sv^{-1}$ in the first two generations, since fetuses and children have the full potential for parenthood. The additional risk in all subsequent generations is equal to the risk in the first two generations (0.01 man-$Sv^{-1}$), giving a total genetic risk from irradiation of the fetus or young child of about 0.02 man-$Sv^{-1}$ The longer expectation of life would make it unwise to take a lethal cancer risk of less than 0.01 man-$Sv^{-1}$, giving a total risk of these serious radiation injuries of 0.03 man-$Sv^{-1}$, about three times greater than that in a general department It will be realised that, for a given examination, the dose to a child is generally less than that to an adult because of his smaller size, making the risk for a given examination in a child less than threefold that of an adult.

## Valuing the Harm

The value put on a human life, in the sense of avoiding premature death, has been widely researched (Mooney, 1981). Examples are given in Table I In the

TABLE I

Estimates of the value of a statistical life (from Jones-Lee, 1985)

| | Value (US$) |
|---|---|
| Compensating wage differentials for workers in risky occupations (USA) | 600 000 |
| Compensating wage differentials for workers in manufacturing occupations (USA) | 5 960 000 |
| Time/safety trade-off in use of pedestrian subways (UK) | 520 000 |
| Compensating wage differentials in industry (UK) | 1 190 000 |
| Compensating wage differentials for construction workers (UK) | 170 000 |
| Purchase of domestic smoke detectors (USA) | 420 000 |
| Sample survey, willingness to pay for transport safety (UK) | 2 370 000 |
| Sample survey, willingness to pay for hypothetical safe cigarette (UK) | 170 000 |
| Time/safety trade-off for car seat belts (USA) | 560 000 |
| Motorway speed/time/fuel trade-off (UK) | 510 000 |

United Kingdom, the Department of Transport values a fatality when assessing possible savings from road schemes at £134 000 (1984 prices) (Weatherburn, 1984). In general it is apparent that most valuations are within a range of about a factor of 10.

Valuing a serious genetic injury, or a fatality, should include a sum to represent human suffering, the loss of earnings and additional medical expenses, and it is plausible that a court of law would value a premature death and a serious genetic injury at not dissimilar levels Roberts et al (1985) equated the value of a premature death with a severe long-term disability, and for the present purpose the authors agree with the ICRP that a radiation death and a serious genetic abnormality can be grouped together as a "serious radiation injury" for valuation purposes

Using a typical risk factor for general populations of 0.01 man-$\text{Sv}^{-1}$, *i e.* one serious radiation injury per 100 man-Sv, the base monetary value recommended by the NRPB of £3000 man-$\text{Sv}^{-1}$ implies that a minimum sum of £300 000 would be allocated to avert a serious radiation injury. This is comparable with the lower range of values in Table I

### *Valuing the man-sievert in radiodiagnosis*

Do we need a $\beta$ factor in medicine? The NRPB says that its valuation scheme is intended to include medical exposures and also that the major rationale for its scheme is to reflect aversion to physical risks rather than anxiety unrelated to the actual level of risk. This would, under the scheme, be a reason for applying, in radiodiagnosis, a factor to give a higher value than £3000 man-$\text{Sv}^{-1}$, because of the relatively high doses often found in diagnostic radiography. The public recognises that diagnostic radiology is, on balance, beneficial and appears to show little anxiety. It seems reasonable, then, to accept that no $\beta$ factor is needed for public disquiet An exception might be made in paediatric and obstetric radiology. An adult makes the decision to be radiographed himself. For a child or fetus the decision is made by a parent, and this can give rise to anxiety.

The dose rate in medical radiography is likely to be important To quote the NCRP (1980):

> "The existence of dose-rate effectiveness factors has long been recognized from clinical experience and from studies of both genetic and somatic effects in experimental animals Specific analyses of the implications of dose rate for the estimation of genetic risks were presented by BEIR (1972) and UNSCEAR (1972, 1977) committees It was concluded that low-LET radiation delivered at high-dose rates is 3 times as mutagenic per unit absorbed dose as it is at low-dose rates This conclusion was based on experiments with mice From the studies on somatic effects on animals, summarized in the present report, the effectiveness per unit dose of low-LET radiation for life shortening and cancer induction is also generally lower at low-dose rates than at high-dose rates The effectiveness per unit dose of high vs low dose-rate exposure ranges from a factor of about 2 to about 10. In other words, linear interpolation from high doses (1 5, 3 5 Gy) and dose rates (> 0.05 Gy $\text{min}^{-1}$) may overestimate the effects of either low doses (0.2 Gy or less) or of any dose delivered at dose rates of the order of 0 05 Gy $\text{y}^{-1}$ or less by a factor of 2 to 10 This factor is referred to as the Dose Rate Effectiveness Factor, or DREF "

The risk rates discussed above relate to low-dose, life-time exposure (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1977). The great majority of radiological examinations give a mean body dose of less than 0 01 Gy (low in this context) but the dose rate is very high for individual organs, often more than 0.01 Gy $\text{s}^{-1}$. While the data do not give a clear-cut picture at low doses, it may be that the DREF is less at low doses than at high doses. This aspect could be considered further but has not explicitly been taken into account in framing the proposals in this paper.

Which annual individual dose should be chosen from the graph (Fig. 1)? To take the effective dose-equivalent for each examination during a year for each patient and to sum these results to obtain the patient's annual exposure would be the most precise method, as each patient's annual exposure, not just each examination, would be taken into account. An approximate method of so doing based on survey statistics is being investigated (Wall, 1986). Another way of approaching the problem is to recognise that the important factor in medical radiation protection is the X-ray unit: so should a larger value of the detriment be given to a barium fluoroscopy unit than a chest unit? The former gives a much higher dose per examination to the patient. On the other hand, the advantages of having a single value of the detriment are considerable. The users and manufacturers will be able to work to a known quantity.

The multiplying factor to be applied based on the NRPB curve, assuming only one is selected, must be a compromise between the more common procedures, carrying a lower individual dose, and the less common procedures, at higher individual doses, taking into account their relative contributions to the collective dose. This should also be modified by the age-related factors for cancer and genetic risks described earlier. The precise numbers for all of these inputs have not yet been determined but, based on the figures given, a value of the man-Sv in the range of £5000–£10 000 would seem reasonable for most purposes.

Doses in paediatric and obstetric departments should be valued at perhaps five times this value (£25 000–£50 000 man-$\text{Sv}^{-1}$), for the reasons given earlier, *i.e.* the combination of increased risk per unit dose and the application of a $\beta$ factor for anxiety.

## HOW MUCH WILL BE SPENT?

When resources are short, a case for spending money should be indisputable. Hospital managers want to see results, not promises of future benefit. The cost of saving a "life" (*i.e.* premature death or a severe congenital abnormality) from medical radiation protec-

TABLE II

Cost of saving a "life" in medical radiation protection

| | % saving in exposure | Cost per "life" saved (£) |
|---|---|---|
| Carbon-fibre material in: | | |
| table top | 10 | 32 000 |
| cassette face | 10 | 25 000 |
| grid facing | 10 | 3500 |
| Fibre grid interface | 10 | 5800 |
| Rare-earth screens | 50 | nil |

tion has been calculated (Russell, 1985) and compares well with other methods of preventing harm (Table II).

The figures in Table II are for short production runs for the manufacture of the items listed, and with large orders the cost of introducing these techniques should fall considerably. Many methods of dose reduction, *e.g.* careful coning of the beam and the use of gonad shields, cost virtually nothing.

In the United Kingdom the Department of Health has drawn particular attention to the importance of reducing patient dose (DHSS, 1985)

*Countries other than the United Kingdom*

Obviously, a developing country should not be expected to spend large sums of money on radiation protection when other health needs, more basic, are unmet, conversely a richer country might spend more. The sum of £5000–£10 000, chosen here as the value of the man-sievert in medicine, lies close to the value of the annual individual gross national product of the United Kingdom. This allows us to suggest a simple generalisation: a country could allocate as the cost of a man-sievert in medical radiography, a value equivalent to the annual individual gross national product. This means that a country richer than the United Kingdom would allocate more than the United Kingdom, a poorer one less. In other countries allowance could be made if the pattern of radiological examinations is significantly different from that in the United Kingdom, *e.g* if fewer, or more, examinations occur in the patient's last illness.

## Discussion

The value of £5000–£10 000 man-Sv$^{-1}$ suggested here is considerably less than the figure derived (Russell, 1985) from the earlier, NRPB (1981) advice. The present figure is more appropriate to medical radiography—the NRPB advice had a larger valuation at high doses, partly resulting from allowance for the dose limits, which do not apply to medical irradiation of patients.

In choosing specific valuations for the man-sievert we do not imply an accurate valuation of the hazard. Rather the estimates are, we feel, the best that can be made with the data available.

Radiology is entering an exciting phase with regard to radiation protection of the patient. It is important that decisions are made on firm ground.

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1987, *The British Journal of Radiology*, 60, 685–692 JULY 1987

# Strontium-89 radionuclide therapy: a dosimetric study using impulse response function analysis

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(*Received October 1986 and in revised form February 1987*)

## ABSTRACT

In a series of patients receiving $^{89}$Sr palliation for metastasised prostatic carcinoma, strontium renal plasma clearance was found to vary from 0.14 to 11.8 l day$^{-1}$, and the extent of skeletal metastatic disease seen on $^{99}$Tc$^{m}$-MDP images varied from a few small metastases to a superscan Using a numerical technique based on impulse response function (IRF) analysis, we have investigated the effect of such variation between patients on $^{89}$Sr dosimetry The whole-body IRF, $H_{WB}(t)$, is defined by the deconvolution of the whole-body strontium retention function, $R_{WB}(t)$, with the plasma retention function, $P(t)$ For patients with minimal metastatic bone disease we assumed $H_{WB}(t) = H_0(t)$, where $H_0$ is the IRF derived from the International Commission on Radiological Protection model for normal strontium metabolism. The strontium plasma clearance, $k$, was allowed to vary, and the resulting variation of $R_{WB}(t)$, $P(t)$ and absorbed dose to bone marrow calculated By convoluting $P(t,k)$ with the IRF measured for a discrete metastasis, the effect of varying $k$ on tumour dose was investigated. Tumour and bone marrow dose were shown to change by a factor of three as $k$ varied over the range observed in patients For patients with extensive metastatic bone disease we assumed $H_{WB}(t) = (1-\beta)H_0(t)+\beta H_s(t)$, where $H_s$ was the IRF measured for a superscan patient and $\beta$ was a parameter reflecting the extent of skeletal metastatic disease The effect of varying $\beta$ on tumour and bone marrow dose was investigated, and dose shown to decrease by a factor of five as $\beta$ increased from zero to unity Impulse response function analysis was found to be a powerful and useful aid in clarifying the relationship between strontium kinetics and $^{89}$Sr dosimetry.

Pecher (1942) was the first to report a possible therapeutic role for the beta-emitting radionuclide $^{89}$Sr in the palliation of disseminated carcinoma of the prostate. Recently, interest in radiostrontium treatment was revived by Firusian et al (1976) and Robinson (1986), and a multicentre clinical trial evaluating $^{89}$Sr therapy is in progress in centres in the USA and the UK. As part of this latter study, we examined strontium kinetics in patients with metastasised prostatic carcinoma (Blake et al, 1986) and are undertaking quantitative studies to determine the absorbed dose delivered to metastases and red bone marrow (Blake et al, 1987). Together with clinical findings and data on haematological toxicity, these studies will provide a comprehensive understanding of $^{89}$Sr therapy for comparison with alternative radionuclide therapies for metastatic bone disease (Eisenhut et al, 1986; Goeckeler et al, 1986; Maxon et al, 1986).

During $^{85}$Sr kinetic studies, we found that strontium renal plasma clearance varied widely among patients receiving $^{89}$Sr therapy and was often significantly reduced compared with values reported in healthy adult men (Blake et al, 1986). A brief summary of these findings is given in the following section of this report. They are of interest because they raise the possibility that, correlated with patient-to-patient variations in renal strontium excretion, there are variations in absorbed dose to metastases and bone marrow that may be significant for the clinical effectiveness of $^{89}$Sr therapy and its associated haematological toxicity.

Among patients referred to our department for radiostrontium therapy, $^{99}$Tc$^{m}$-MDP images showed wide variations in the extent of metastatic disease in the skeleton, ranging from fewer than five small, discrete deposits (five of 27 patients) to superscan studies showing essentially complete skeletal involvement (four of 27 patients) (McEwan et al, 1986) As with the differences in strontium renal clearance, it is of interest to examine what effect the extent of metastatic disease in the skeleton has on absorbed dose to tumour and bone marrow. Both these questions may be investigated using the technique of skeletal impulse response function (IRF) analysis described by Reeve and Hesp (1976). In this present paper, we report the results of a study of $^{89}$Sr dosimetry based on the methods of Reeve and coworkers.

## STRONTIUM RENAL PLASMA CLEARANCE

Before describing the method of numerical analysis used, we look briefly at the range of values for strontium renal plasma clearance found in patients with metastatic bone disease Over a period of 18 months, 27 patients with bone pain due to disseminated prostatic carcinoma received $^{89}$Sr therapy in the Department of Nuclear Medicine, Southampton General Hospital; 22 patients were well enough to give a 24 h urine collection

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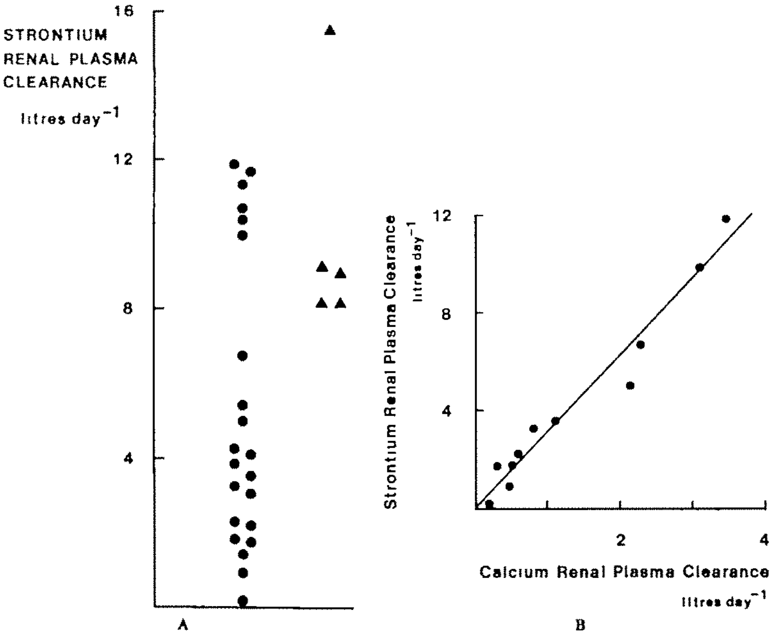

FIG 1

(A) Measurements of strontium renal plasma clearance ● values in 22 patients with disseminated prostatic carcinoma, ▲ values in five healthy adult men measured by Harrison & Sutton (1967). (B) Plot of strontium renal plasma clearance against calcium plasma clearance for 11 of the patients shown in (A) The solid line is the linear regression fit $k_{Sr} = 3.1\,k_{Ca} + 0.1$

after treatment. Strontium renal plasma clearance was calculated using the equation:

$$k_{\text{renal}} = \frac{\int_t^{t+24} \mathrm{d}U}{\int_t^{t+24} P\,\mathrm{d}t}\ \mathrm{l\ day^{-1}} \qquad (1)$$

where the numerator is the urinary strontium excretion in a 24 h period expressed as a fraction of administered activity and the denominator is the time integral of the fractional strontium retention in 1 l of plasma. A full description of the technique used has been given by Blake et al (1986). Measured values of $k_{\text{renal}}$ varied from 0.14 to 11.8 l day$^{-1}$ (Fig 1A) and were frequently low compared with values reported for healthy adult men (Harrison & Sutton, 1967). In 11 patients, calcium renal plasma clearance was measured at the same time as strontium clearance. Calcium and strontium clearances showed a highly significant linear correlation (Fig. 1B, Spearman rank correlation coefficient $R = 0.991$, $p < 0.001$).

## METHODS

### *Impulse response function analysis*

Impulse response function analysis is widely applied to the study of functional data in nuclear medicine and a comprehensive review has recently been published by Szabó et al (1985). The application to skeletal strontium kinetics described in the present report is based on a numerical technique used by Reeve and coworkers (Reeve et al, 1976a,b; Reeve & Hesp, 1976) Definitions of the mathematical symbols we use are summarised in Table I

Let $R_{WB}(t)$ be the fractional total-body retention of intravenously administered $^{89}$Sr at time $t$, $P(t)$ the fractional retention in 1 l of plasma and $H_{WB}(t)$ the total-body IRF. $H_{WB}(t)$ is defined by the integral equation:

$$R_{WB}(t') = \int_0^{t'} P(t)\,H_{WB}(t'-t)\,\mathrm{d}t \qquad (2)$$

The basic concept behind Equation 2 can be explained as follows $P(t)$ is the tracer input function to the body and $H_{WB}(t)$ is defined as the retention function for a hypothetical unit impulse of tracer in plasma, with reutilisation of tracer following re-entry into the blood-

TABLE I

DEFINITIONS OF MATHEMATICAL SYMBOLS

| | |
|---|---|
| $R_{WB}$ | Total-body strontium retention function |
| $R_B$ | Retention function for the skeleton |
| $R_T$ | Retention function for a discrete metastasis |
| $P$ | Retention function for unit volume of plasma |
| $H_{WB}$ | Total-body IRF |
| $k$ | Net strontium plasma clearance constant |
| $k_{\text{renal}}$ | Renal component of $k$ |
| $k_{\text{gut}}$ | Gut component of $k$ |
| $H_0$ | Total-body IRF for a person with a normal skeleton |
| $H_T$ | IRF for a discrete metastasis |
| $H_S$ | Total-body IRF for a person with metastatic involvement of the entire skeleton |
| $\beta$ | Fraction of $H_S$ assumed to be present in $H_{WB}$ |
| $\tau$ | Mean life for $^{89}$Sr decay |
| $D_{RM}$ | Mean absorbed dose to red bone marrow |
| $D_T$ | Mean absorbed dose to a metastasis |

stream eliminated (Reeve & Hesp, 1976). If the plasma input is considered to consist of a continuous sequence of elementary impulses, then the net retention at any time, $R_{WB}(t)$, is the sum of the tracer retained from each preceding elementary input. The dependence of $R_{WB}(t)$ on the plasma curve is thus made explicit, and it is evident that $H_{WB}(t)$ is the most fundamental way of representing strontium retention in the body. The validity of Equation 2 depends on assumptions of linearity and time invariance that are discussed in detail in the review of Szabó et al (1985). We shall discuss later the validity of the time-invariance assumption in cases of progressive metastatic disease. Finally, we note that, in analogy with Equation 2, a similar integral equation can be written that defines an IRF for any selected part of the body, for example, the skeleton alone, any discrete metastasis, or any chosen area of bone.

*Numerical methods*

For the purpose of numerical modelling, Equation 2 was written as the sum of discrete terms:

$$R_{WB}(j) = \sum_{i=1}^{j} P(i)\, H_{WB}(j+1-i)\, \Delta t \qquad (3)$$

where time $t$ and the running integer $i$ are related through the step increment in time $\Delta t$:

$$t = (i-1)\, \Delta t \qquad (4)$$

Given measured functions for $R_{WB}(i)$ and $P(i)$, Equation 3 can be solved for $H_{WB}(i)$ using the technique of matrix deconvolution to obtain the following set of iterative equations (Reeve et al, 1976a).

$$H_{WB}(j) = P^{-1}(1)\left\{\frac{R_{WB}(j)}{\Delta t} - \sum_{i=2}^{j} P(i)\, H_{WB}(j+1-i)\right\} \qquad (5)$$

To study the problems of $^{89}$Sr dosimetry discussed above, we need to achieve the reverse of Equation 5: that is, given a known function for $H_{WB}$, can $R_{WB}$ and $P$ be calculated? It was shown by Reeve and Hesp (1976) that one element in solving this latter problem is obtained by rewriting Equation 5 to give:

$$P(j) = H_{WB}^{-1}(1)\left\{\frac{R_{WB}(j)}{\Delta t} - \sum_{i=1}^{j-1} P(i)\, H_{WB}(j+1-i)\right\} \qquad (6)$$

so that $P$ is expressed in terms of $H_{WB}$ and $R_{WB}$.

A second essential equation is obtained by considering the elimination of strontium from the body. Excretion of $^{89}$Sr occurs through the kidneys and the gut at a rate proportional to plasma concentration, giving the further relationship:

$$\frac{dR_{WB}(t)}{dt} = -k\, P(t) \qquad (7)$$

where the net strontium plasma clearance, $k$, is the sum of renal and gut contributions ($k = k_{\mathrm{renal}} + k_{\mathrm{gut}}$). In the healthy adult, 80% of strontium excretion is renal (Harrison & Sutton, 1967; Marshall et al, 1973). The validity of Equation 7 was verified in studies by Harrison et al (1955). Physiologically, the relation arises because at levels of total chemical strontium administered during $^{89}$Sr therapy, strontium excretion is treated as an infinitesimal increment in serum calcium concentration (Comar, 1967). Thus strontium plasma clearance remains constant provided calcium homeostasis remains in a stationary state. In the notation of Equations 3 and 4, Equation 7 may be written:

$$R_{WB}(j) = R_{WB}(j-1) - k\, \Delta t\, P(j-1) \qquad (8)$$

If it is assumed now that $H_{WB}(i)$ and $k$ are known, Equations 6 and 8 can be solved iteratively as coupled equations to find $R_{WB}(i)$ and $P(i)$. The use of this computational technique to investigate how the absorbed dose to bone marrow and metastases varies with strontium plasma clearance and the extent of metastatic bone disease is discussed in the following sections.

*Bone marrow dosimetry and strontium plasma clearance*

We examined first how $R_{WB}(t)$, $P(t)$ and the absorbed dose to bone marrow, $D_{RM}$, depend on $k$ for patients whose metastatic bone disease is limited to a few small metastases In such individuals with negligible skeletal involvement we assumed that $H_{WB}$ approximates to the IRF for a person with a normal skeleton, $H_0$. $H_0$ was calculated from Equation 5 using for total-body and plasma retention the normal functions adopted by Marshall et al (1973):

$$\left.\begin{aligned} &R_{WB}(t) = 0.6\,(1+5t)^{-0.18} + 0.4\,\mathrm{e}^{-0.25t} \\ &P(t) = k^{-1}\,\{0.54\,(1+5t)^{-1.18} + 0.1\,\mathrm{e}^{-0.25t}\} \\ &k = 10.4\ \mathrm{l\ day^{-1}} \end{aligned}\right\} \qquad (9)$$

These equations have been simplified by omitting a slowly varying term for bone resorption, the contribution of which is negligible on the time scale of $^{89}$Sr decay. In $^{85}$Sr total-body retention studies in patients receiving $^{89}$Sr therapy, we found that for individuals with limited skeletal involvement, measured total-body retentions often agreed closely with Marshall's normal function, making it an appropriate choice for the calculation of $H_0$ (Blake et al, 1986).

Equations 9 were evaluated for $R_{WB}(t)$ and $P(t)$ at intervals of 0.05 days for $0 < t < 100$ days, and $H_0(t)$ found by matrix deconvolution. Equations 6 and 8 were then used to calculate new total-body and plasma retention functions, $R_{WB}(t,k)$ and $P(t,k)$, for values of $k$ between 1.0 and 15.0 l day$^{-1}$. To calculate bone marrow dose following $^{89}$Sr administration, we need to find the component of $R_{WB}$ retained in the skeleton, $R_B$. Reeve and Hesp (1976) assumed that total-body strontium is all retained in the skeleton except for a small fraction in the extracellular fluid (ECF) in equilibrium with plasma strontium, giving the relationship:

$$R_B(t,k) = R_{WB}(t,k) - V_{ECF}\, P(t,k) \qquad (10)$$

where $V_{ECF}$ is the effective volume of ECF. We calculated $R_B(t,k)$ from Equation 10 assuming $V_{ECF} = 16.25$ l, the value adopted in the strontium kinetic model of Marshall et al (1973), and in good agreement with our own studies of plasma strontium curves (Blake et al, 1986). Finally, the function $R_B(t,k)$ was used to evaluate the scaling of bone marrow absorbed dose with $k$ by calculating the time integral of $^{89}$Sr activity in the skeleton

$$D_{RM}(k) = C_{RM} \int_0^\infty R_B(t,k)\, e^{-t/\tau}\, dt \qquad (11)$$

where the exponential term corrects for the radioactive decay of $^{89}$Sr and $C_{RM}$ is a constant term which may be evaluated using the International Commission on Radiological Protection (ICRP) model for bone dosimetry (ICRP, 1979). We shall show later that our conclusions for the scaling of $^{89}$Sr dosimetry with plasma clearance are extremely insensitive to the assumptions behind Equation 10, which we introduced for computational convenience.

*Tumour dosimetry and strontium plasma clearance*

We examined next how the strontium retention curve for a skeletal metastasis, $R_T(t)$, and the mean absorbed dose to the metastasis, $D_T$, depend on $k$, again considering the case of a patient with minimal skeletal metastatic disease, so that plasma curves approximated to the functions $P(t,k)$ calculated above. Let $H_T(t)$ be the IRF for the metastasis. Strontium retention in the metastasis was calculated using the following equation (compare Equation 2):

$$R_T(t',k) = \int_0^{t'} P(t,k)\, H_T(t'-t)\, dt \qquad (12)$$

The function $R_T(t,k)$ was then used to evaluate the scaling of the absorbed dose to tumour with $k$ by calculating the time integral of $^{89}$Sr activity in the metastasis:

$$D_T(k) = C_T \int_0^\infty R_T(t,k)\, e^{-t/\tau}\, dt \qquad (13)$$

where $C_T$ is a constant term whose value depends on the $^{89}$Sr activity administered to the patient, the mean beta-particle energy for $^{89}$Sr and the mass of bone, tumour and residual marrow in the metastasis (Blake et al, 1987).

The tumour IRF, $H_T$, used in these calculations was found from $^{85}$Sr scintigraphic studies of metastatic strontium retention in a patient with a skeletal deposit that appeared to involve uniformly a lower dorsal vertebra (Blake et al, 1986,1987). Over the period $0 < t < 100$ days following $^{89}$Sr therapy, retention in this metastasis was found to be closely fitted by the function

$$R_M(t) = 2.4\,(1 - e^{-2.3t})\, e^{-0.0034t} \text{ per cent} \qquad (14)$$

Plasma data for this patient showed a close fit to the normal plasma curve $P(t, k)$ for $k = 5.0$ l day$^{-1}$. $H_T$ was calculated by deconvolution of $R_M(t)$ with $P(t,5)$.

*Strontium-89 dosimetry and extent of skeletal metastatic involvement*

Let $H_S(t)$ be the total-body IRF of a patient with metastatic involvement of the entire skeleton. Our studies of strontium kinetics in patients receiving $^{89}$Sr therapy included three whose $^{99}$Tc$^m$-MDP images fulfilled the superscan criterion (Blake et al, 1986). In the most extreme case, bone scintigraphy showed intense $^{99}$Tc$^m$ uptake with uniform involvement of the spine, pelvis, ribs, shoulder girdle, femora, humeri and skull and extensive involvement of the distal extremities. This patient approximated to the case of total skeletal involvement, and the total-body and plasma retention data were deconvoluted to obtain a representative curve for $H_S$.

For patients with an intermediate degree of skeletal involvement (between the extreme cases of negligible metastatic disease and the prostatic superscan) we assumed that strontium kinetics were determined by an IRF of the form.

$$H_{WB}(t) = (1-\beta)\, H_0(t) + \beta\, H_S(t) \qquad (15)$$

Equation 15 assumes that in such individuals a fraction, $\beta$, of the skeleton is characterised by the IRF $H_S$ and the remainder by $H_0$. The equation was used to substitute for $H_{WB}$ in Equation 6, which was then solved with Equation 8 using a range of values of $\beta$ and $k$ to find $R_{WB}(t,k,\beta)$ and $P(t,k,\beta)$. The effect of $\beta$ on the tumour dose was examined by convoluting $P(t,k,\beta)$ with $H_T(t)$ to find $^{89}$Sr retention in metastatic bone and hence, by Equation 13, the integrated absorbed dose. To investigate the effect of $\beta$ on the absorbed dose to red bone marrow we assumed that the most informative figure would be the dose averaged over uninvolved marrow only, excluding areas already compromised by tumour spread. The latter will vary from patient to patient, making an exact calculation impossible. However, as a rough indication of the effect that might be expected, we estimated marrow dose by convoluting $P(t,k,\beta)$ with $H_0(t)$, assuming that the dose required is the same as the marrow dose averaged over a normal skeleton following the given plasma retention function.

## RESULTS

*Strontium-89 dosimetry and strontium plasma clearance*

The variation of strontium plasma clearance in patients with minimal skeletal metastatic disease was found to cause large changes in total-body (Fig. 2A) and metastatic (Fig. 2C) strontium retention. As $k$ decreased from 15 to 2.1 day$^{-1}$, the 100-day total-body retention increased from 14% to 57% and metastatic retention from 0.7% to 2.9%. Metastatic retention correlated closely with retention in the normal skeleton. The variation of plasma retention was examined by plotting the ratio of $P(t,k)$ to the standard plasma curve of

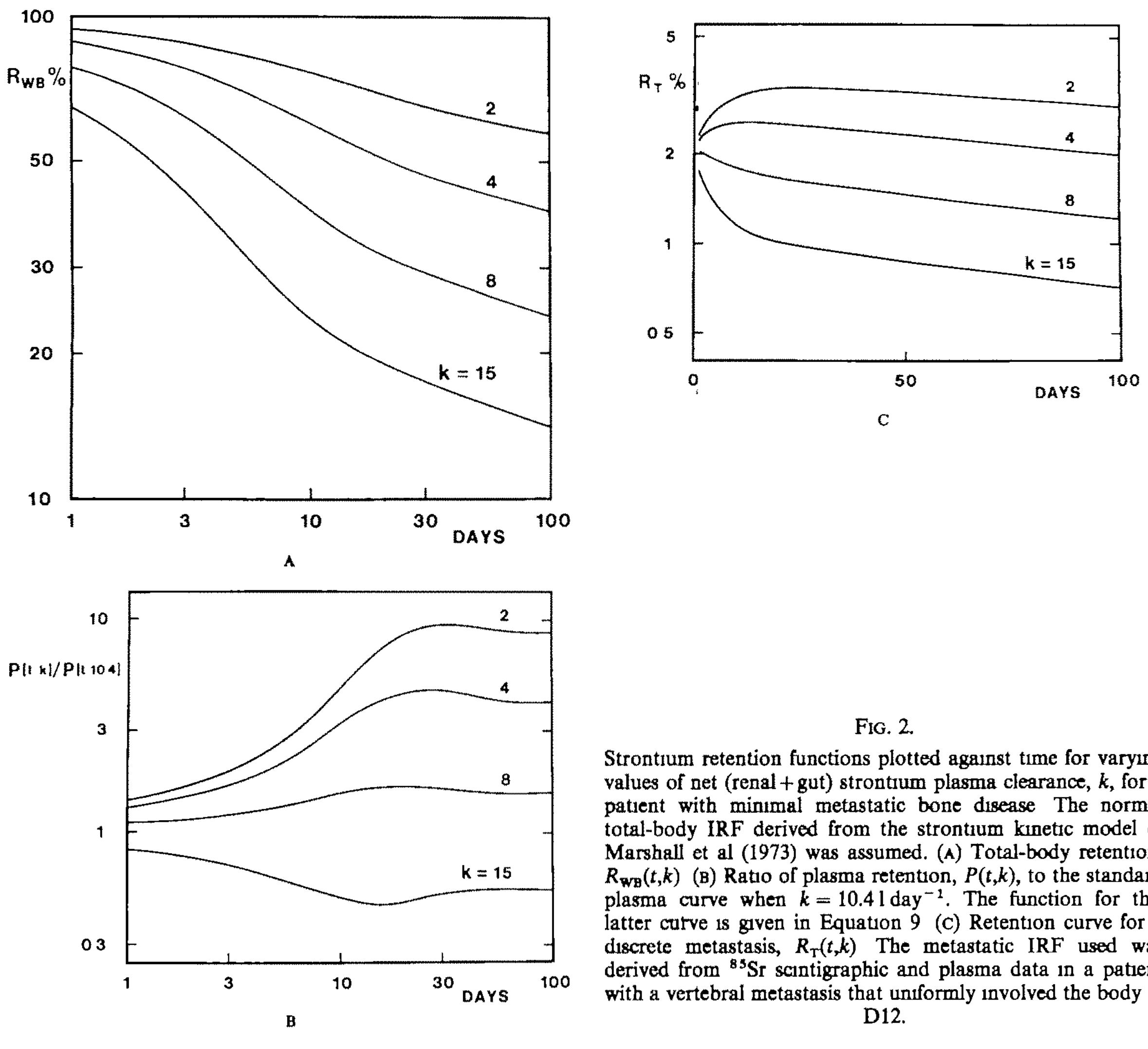

FIG. 2.

Strontium retention functions plotted against time for varying values of net (renal + gut) strontium plasma clearance, $k$, for a patient with minimal metastatic bone disease. The normal total-body IRF derived from the strontium kinetic model of Marshall et al (1973) was assumed. (A) Total-body retention, $R_{WB}(t,k)$ (B) Ratio of plasma retention, $P(t,k)$, to the standard plasma curve when $k = 10.4\,\mathrm{l\,day^{-1}}$. The function for this latter curve is given in Equation 9 (C) Retention curve for a discrete metastasis, $R_T(t,k)$ The metastatic IRF used was derived from $^{85}$Sr scintigraphic and plasma data in a patient with a vertebral metastasis that uniformly involved the body of D12.

Marshall et al (Equation 9) as a function of time (Fig. 2B). During the first day after strontium administration, plasma strontium retention was found to be insensitive to $k$, but thereafter the plasma curves diverge, the ratio to the standard model reaching a plateau value after about 1 month. At this time the plasma ratio varied from 0.5 for $k = 15\,\mathrm{l\,day^{-1}}$ to 9 for $k = 2\,\mathrm{l\,day^{-1}}$. The effect of plasma clearance on $^{89}$Sr dosimetry for bone marrow and metastases was examined by normalising $D_{RM}(k)$ and $D_T(k)$ to their values at $k = 10.4\,\mathrm{l\,day^{-1}}$ (the normal value of Marshall et al (1973)) and plotting this ratio as a function of $k$. The dose ratio was found to follow the same curve for both $D_{RM}$ and $D_T$ (Fig. 4, curve labelled $\beta = 0$). The ratio varied from 0.75 for $k = 15\,\mathrm{l\,day^{-1}}$ to 2.5 for $k = 2\,\mathrm{l\,day^{-1}}$.

### *Strontium-89 dosimetry and extent of skeletal metastatic disease*

The changes in total-body, plasma and metastatic strontium retention as the parameter $\beta$ (quantifying the extent of skeletal metastasis) varied between zero and unity are shown in Fig 3 for the case $k = 5\,\mathrm{l\,day^{-1}}$. This value of $k$ was chosen as representative for patients in whom renal plasma clearance was significantly depressed (Fig. 1A). Total-body retention increased with $\beta$ (Fig. 3A), whereas plasma and metastatic retention decreased up to 10-fold (Fig. 3B,C). Absorbed doses to bone marrow and metastasis were normalised to their values when $\beta = 0$ and $k = 10.4\,\mathrm{l\,day^{-1}}$, and dose ratio as a function of $\beta$ and $k$ is shown in Fig. 4. For the solitary vertebral metastasis, used for the calculation of $H_T$, $H_T/H_S \sim 0.005$, suggesting that for a typical patient

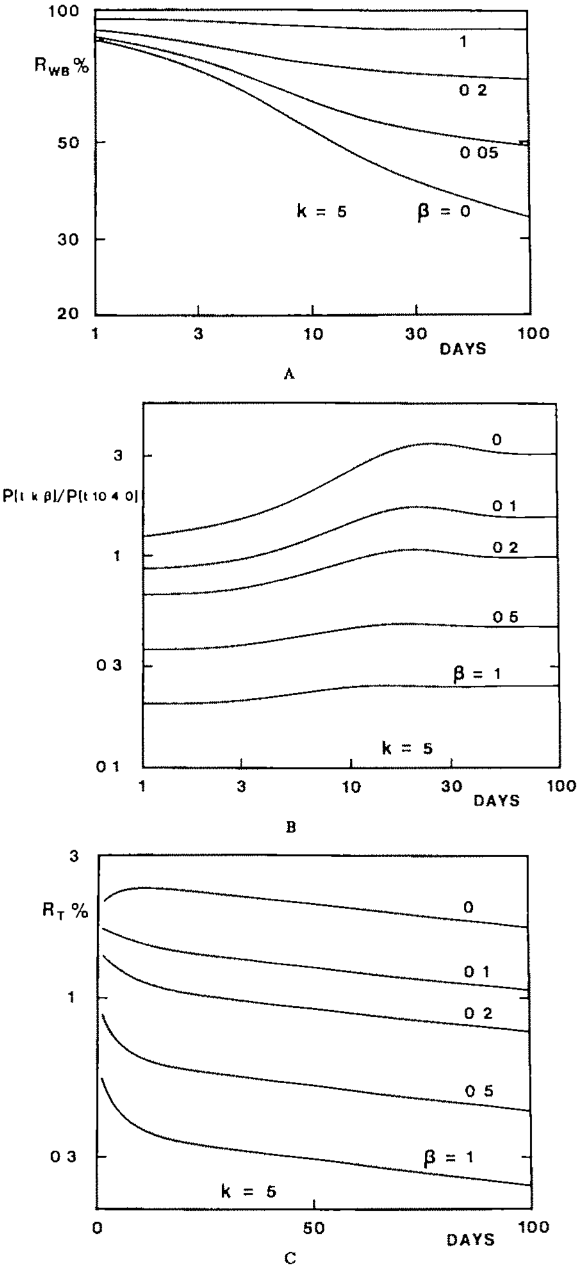

FIG 3.

Strontium retention functions plotted against time for varying extent of skeletal metastatic involvement $0 < \beta < 1$ in a patient with net plasma clearance $k = 5$ l day$^{-1}$. A total-body IRF of the form $H_{WB} = (1-\beta)H_0 + \beta H_S$ was assumed, where $H_0$ and $H_S$ are respectively the normal function used in Fig 2 and the function determined for a patient with a prostatic superscan. For $t > 10$ days, $H_S/H_0 \sim 15$. (A) Total-body retention, $R_{WB}(t,k,\beta)$ (B) Ratio of plasma retention $P(t,k,\beta)$ to the standard curve with $k = 10.4$ l day$^{-1}$ and $\beta = 0$. (C) Retention curve from a discrete metastasis, $R_T(t,k,\beta)$ The same metastatic IRF was used as in Fig 2(c)

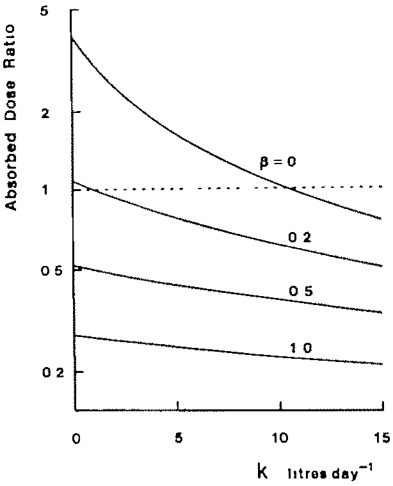

FIG. 4

Scaling of absorbed dose to red bone marrow and tumour following $^{89}$Sr therapy with net strontium plasma clearance, $k$, and extent of skeletal metastatic disease, $\beta$ Absorbed dose was normalised to the dose when $\beta = 0$ and $k = 10.4$ l day$^{-1}$. Curves for bone marrow and metastasis were, essentially, identical. Because all physically reasonable IRFs are slowly varying over the mean life of $^{89}$Sr, the dose ratio curves shown are insensitive to the exact choice of IRFs for metastases and normal bone

with extensive multiple metastases confined to spine and pelvis, one can expect $\beta \sim 0.05$–$0.1$. The superscan patient with $\beta \sim 1$ is an exceptional case

## DISCUSSION

The results of this numerical study of $^{89}$Sr dosimetry are indicative only of the direction and approximate magnitude of changes in total-body, plasma and metastatic strontium retention and absorbed dose which arise from patient-to-patient variations in plasma clearance and extent of metastatic disease in the skeleton. The detailed numerical results depend on $H_0$, $H_T$ and $H_S$, and while we have endeavoured to choose appropriate functions based on strontium kinetic studies in patients receiving $^{89}$Sr therapy, individual variations undoubtedly occur. Despite this limitation, many of the findings of IRF analysis agree well with our published kinetic data (Blake et al, 1986), leading us to believe that the results reported here are at least qualitatively correct.

Our dosimetric studies were made on the assumption of time invariance of the IRF, a condition inconsistent with the progressive nature of metastatic bone disease. However, we were able to repeat total-body strontium retention studies in five patients who required further radiostrontium therapy at intervals of 6–9 months after their initial treatment and in only one patient was a detectable change in $R_{WB}(t)$ found. It is evident from

Figs 2 and 3 that the critical factor in determining absorbed dose is the convolution of the plasma curve with the IRF over the first 2 or 3 weeks following therapy, and it seems likely that in the majority of patients the rate of progression of disease is at least one or two orders of magnitude too slow to affect our conclusions significantly.

An important finding during our numerical studies was that the dependence of dose ratio on $k$ and $\beta$, shown in Fig. 4, was essentially identical for bone marrow and metastasis, despite differences in the IRF for normal and metastatic bone. This result was confirmed when virtually identical dose ratios were calculated for a variety of trial functions for $H_T$. Physically, it arises because, over the time scale set by $^{89}$Sr decay, all realistic functions for $H$ are rather similar slowly varying functions of time. This finding is important to our conclusions for two reasons: (i) scaling of tumour dose with $k$ and $\beta$ is insensitive to patient-to-patient variation in $H_T$; (ii) scaling of bone marrow dose with $k$ and $\beta$ is insensitive to differences in the IRF for trabecular and cortical bone and to any differences in skeletal IRF that arise from the choice of strontium kinetic model for dividing total-body strontium between bone and soft-tissue compartments

Our studies of strontium plasma clearance measured only the renal component (Fig. 1A). However, comparison of total-body and plasma retention data obtained from patients with those from Fig. 2 showed that good agreement with the theoretical curves was obtained by adding $k_{gut} \sim 2$ l day$^{-1}$ to measured values of $k_{renal}$. This figure for $k_{gut}$ is consistent with reported normal values (Harrison & Sutton, 1967; Marshall et al, 1973). Whereas a reasonable estimate of the parameter $k$ can be obtained from strontium (Fig. 1A) or calcium (Fig 1B) renal clearance data, the definition of the factor $\beta$ (the parameter defining the extent of skeletal metastatic disease) is dependent on strontium kinetic data for each particular superscan patient. Our studies of plasma curve data (Blake et al, 1986) suggest that a convenient empirical estimate of the likely reduction in absorbed dose due to extent of disease can be obtained from the ratio of the measured 4 h plasma concentration to the normal value predicted from Equation 9. At this time, plasma strontium concentration is dependent on $\beta$ but is insensitive to $k$.

The results of our investigation deal only with how $^{89}$Sr dosimetry scales with $k$ and $\beta$, not with actual absorbed dose figures. In a separate study, it was shown that when the strontium kinetic model of Reeve et al (Equation 10) is combined with the total-body and plasma retention functions of Marshall et al (Equation 9), a figure for the mean absorbed dose to red bone marrow of 2 1 cGy MBq$^{-1}$ is obtained (Blake et al, 1987). This is the absorbed-dose figure corresponding to the point $\beta = 0$, $k = 10.4$ l day$^{-1}$ used for the normalisation of dose ratio in Fig. 4. For the spinal metastasis used in the calculation of $H_T$, a mean tumour dose of 24 cGy MBq$^{-1}$ was found The patient in whom this measurement was made lay at the point $\beta \approx 0$, $k \approx 5$ l day$^{-1}$ in Fig. 4.

Finally, we examine some implications of our study for $^{89}$Sr therapy. Absorbed dose to metastases and bone marrow scale in a virtually identical manner, showing that no therapeutic advantage arises as $k$ and $\beta$ vary. Patients receiving the highest dose are those with minimal metastatic disease and low values of $k$. They may be identified from bone scintigraphy and calcium renal plasma clearance (Fig. 1B) before therapy. In patients with extensive disease, dose is reduced and is less dependent on variation in $k$. In the case of superscan patients, a radiotherapeutic effect would seem unlikely without the use of considerably increased $^{89}$Sr activity. An interesting clinical issue is whether patients with extensive metastatic disease show more severe haematological toxicity than those with minimal involvement, following equal treatment activities. This effect might be expected because: (i) bone marrow reserve in patients with extensive disease is more likely to be compromised by tumour spread; (ii) residual functioning marrow within metastatic bone receives an absorbed dose an order of magnitude larger than marrow associated with the normal skeleton; (iii) extensive metastatic bone disease correlates (albeit weakly) with lower values of $k_{renal}$. In practice, patients with extensive disease show comparable haematological toxicity to those with limited disease (McEwan et al, 1986). This observation may arise because in patients with severely compromised marrow the site of haemopoiesis could include areas in the long bones and extramedullary sites protected from irradiation by $^{89}$Sr beta rays. Impulse response function analysis suggests that a further contributory factor in mitigating the adverse factors enumerated above is decreased strontium uptake in normal bone in patients with extensive metastatic bone disease.

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# Validation of a digital videodensitometric program analysis for measurement of left ventricular ejection fraction

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(*Received October 1986*)

## ABSTRACT

Left ventricular (LV) function was studied in 30 patients using digital subtraction angiography by the intravenous approach. Each ventriculogram was processed with a specific videodensitometric analysis to determine LV ejection fraction The program was verified in an experimental set-up consisting of nine latex balloons filled with contrast medium. Its validation has been established by comparing videodensitometric results with classical results supplied by geometric methods A good correlation was obtained ($r = 0.9449$) and, furthermore, with experimental models, videodensitometric analysis seemed to be more accurate than geometric analysis. Digital videodensitometry appears to be a valuable and accurate method for quantifying LV function, and a promising technique for determination of the real volumes.

Digital subtraction angiography enhances standard angiographic images by processing the video signal through a high-speed computer. Several studies have already reported excellent results concerning left ventricular (LV) volumes and ejection fraction (EF) measurements achieved through digital subtraction angiography (DSA) Nevertheless, all of the data were based on classical geometric assumptions for the left ventricle (Sandor et al, 1979; Tobis et al, 1982; Pernes et al, 1985).

Several previous attempts have been made, using densitometric techniques and analysing analog images from 35 mm cine film, to study LV function (Dumesnil et al, 1974; Erikson et al, 1978, 1980), or to determine vessel diameter (Silverman, 1971; Serruys et al, 1984). To date, few investigators have reported their results concerning the quantification of LV function by densitometry using DSA (Spiller et al, 1983; Tobis et al, 1983; Greenbaum & Evans, 1984). Digital videodensitometry appears to be a promising method of quantifying LV function, because the limitations of geometric assumptions regarding the ventricular chamber can be disabling when the symmetry of the cavity is lost following coronary artery disease.

In this paper, we have developed a systematic approach to using videodensitometry for processing LV digital angiograms obtained following intravenous injection of contrast medium. The validation of the results was achieved by comparing LV volumes and ejection fractions with those determined by a conventional quantitative geometric technique.

## MATERIALS AND METHODS

Videodensitometric studies were carried out by two different methods: the first an experimental model and the second a radiological/clinical setting involving 30 ventriculograms recorded in the usual manner at our institution.

### *Experimental model*

Before applying the videodensitometric technique to angiograms, we tested the procedure experimentally. Imaging phantoms consisting of nine latex balloons were inflated, using an automatic injector, with known volumes of contrast medium of different iodine concentrations. For each balloon, two different volumes were obtained to simulate a "diastolic" (large volume) and a "systolic" (small volume) measurement.

The first three balloons were inflated with contrast medium at 5% iodine concentration; the other six were filled with contrast medium with different iodine concentrations (2%, 3%, 5%). One of these (Case 3) was distorted to resemble an hourglass shape.

The filled balloons were submerged in a water-filled vat and then imaged with a DSA system. Once acquired, the images were finally processed by videodensitometric analysis to determine a simulated ejection fraction measurement (SEF).

### *Clinical protocol*

Thirty patients (21 males and nine females) with a mean age of 45 years (range 17–73 years) were investigated using DSA equipment manufactured by CGR (Divas). The indications for cardiac DSA were as follows: 20 patients were examined for myocardial ischaemia, two for aortic disease, seven for severe hypertension and one for a non-ischaemic cardiomyopathy.

For each patient a special-purpose 5 F catheter was introduced percutaneously into a superficial vein in the antecubital fossa, and the tip was positioned in the right atrium. The contrast medium used was sodium and meglumine ioxaglate (Hexabrix, Guerbet Laboratories) in a dose of 40 $cm^3$ per patient at a rate of 20 $cm^3/s$

The radiographic images were acquired at 25 images/s using a 23 cm image intensifier field, and digitised in a 256 × 256 × 8-bit matrix.

To improve the accuracy of the results the linearity of the X-ray chain was checked, as previously emphasised by others (Simons & Kruger, 1985) The acquisitions were electrocardiogram (ECG)-triggered to separate end-diastolic images (EDI) (as those obtained at the top of the R-wave) from end-systolic images (ESI) (visually selected as the smallest areas in the cardiac cycle). The image acquisitions were made by storing the digital but non-processed data in a high-capacity memory (16 Mbyte) and then transferring these images to a 300 Mbyte hard disk

The ECG-synchronised temporal mask mode subtraction was used to obtain the final processed images. Only two subtracted images were selected (one EDI and one ESI) for processing by means of the videodensitometric program. For geometric quantification, LV analysis of angiograms was undertaken using the single-plane method of Brun et al (1972), which is derived from Chapman's biplane method.

*Basic concept of the videodensitometric technique*

To apply the videodensitometric technique the previously selected DSA images were recorded on a U-matic video recorder. This was necessary because the videodensitometric program worked in a non-commercial image analysis system, independently installed at a distance from the acquisition equipment (Fig. 1). The signal was then redigitised and processed, using this specific chain, in a 512 × 512 × 8-bit matrix. Even if the signal transfer between both sets of equipment entailed a degradation of the information, in practice, control measures and scale corrections gave results with an error of less than 2%.

A "false colour" interface was designed in order to display on a colour monitor the shades of grey corresponding to the contour of the opacified LV cavity, or of the fluid-filled balloons.

For calculations and physical corrections we have assumed, as described by the Lambert Beer law (Fig. 2), that the difference in attenuation coefficient was directly related to the difference between the logarithms of two images: one before (mask image) and one after injection of contrast medium.

The value, $N$, of a pixel in a subtracted image resulting in the difference of the two image logarithms could be expressed as follows.

$$N = v/\Delta\mu \qquad (1)$$

where $\Delta\mu$ represents the difference between the linear attenuation coefficient of the contrast medium and that of the tissues, and $v$ is the thickness of the vessel. This relationship means that, if we consider a particular point on an image, the logarithmic subtraction between a pixel value of the image before injection of contrast medium $[L_n(I_1)]$ and the value of the same pixel after injection of contrast medium $[L_n(I_2)]$, gives a value of $N$ proportional to the thickness ($v$) of the object at this point. The proportionality constant $\Delta\mu$ depends mainly on the concentration of the contrast medium and the X-ray energy.

In practical terms, if we radiograph a spherical solid we can assume that the thickness of a section penetrated by the X-ray beam is represented by all pixel values

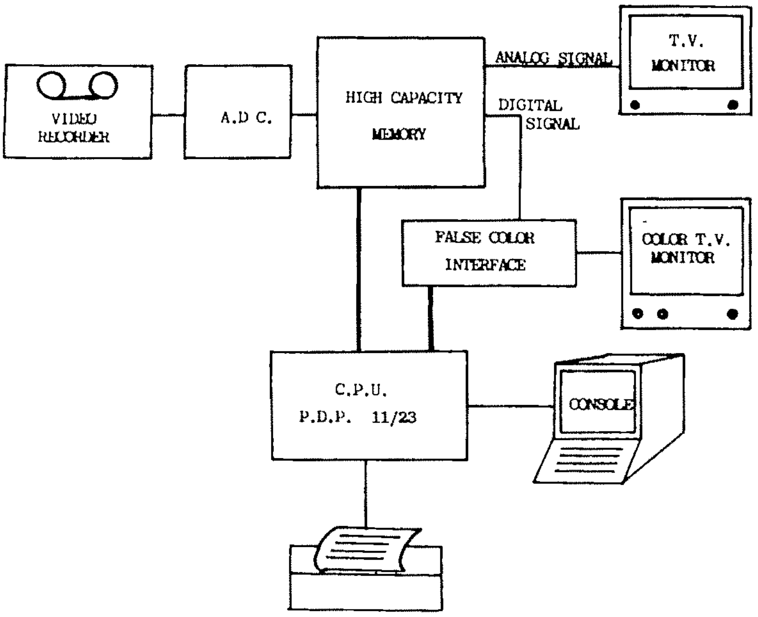

Fig 1

Diagram of the non-commercial equipment used for videodensitometric analysis.

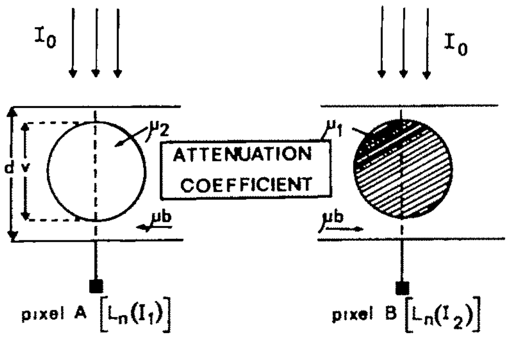

FIG. 2

Left image before injection of the contrast medium; right: after injection of contrast medium. The logarithmic subtraction between two pixels (A and B) included in these images gives a new value, $N = v\Delta\mu$, where $\Delta\mu = \mu_2 - \mu_1$

distributed along a projected diameter, which correspond to a density profile (Fig. 3). If the thickness ($v$) of this sphere, measured at a point P in the direction of the X-ray beam, is proportional to its pixel value, $N$, the volume of the solid will be proportional to the sum of all pixel values included in its projected area. The proportionality coefficient is then represented by the value ($S_E$) of the elementary area of each pixel. The calculation of the volume is, in turn, derived by cutting the solid into cross-sectional areas In this way, all pixel values along the length of a slice represent the density profile, which can be assimilated to the amplitude of the third dimension of the sphere (Fig. 4).

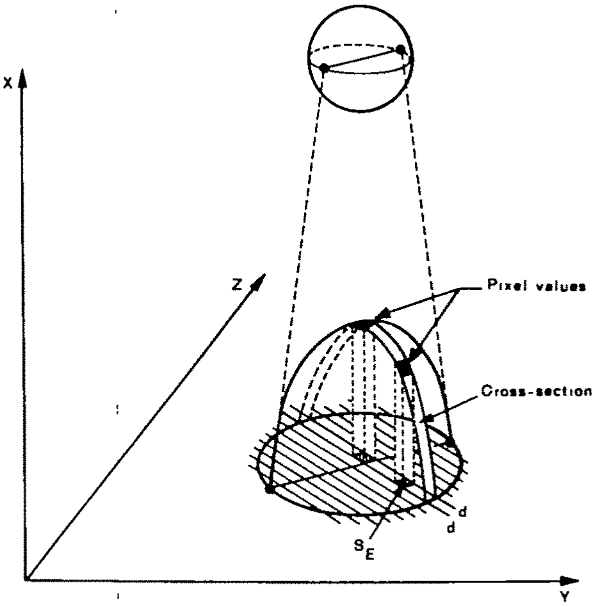

FIG 4.

All pixel values on a density profile correspond to a cross-sectional area included between d and d′ lines. $S_E$ is the projected pixel area

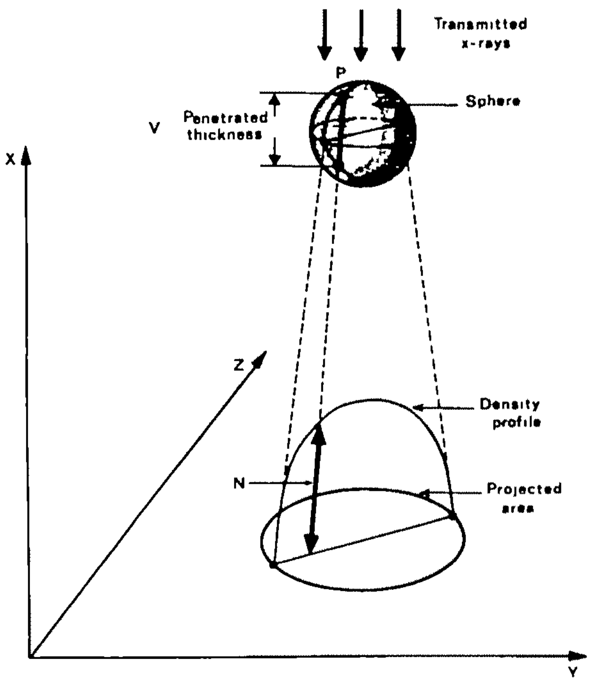

FIG 3.

Projected area of a sphere penetrated by X-rays The penetrated thickness ($v$) of the sphere at point P can be represented by the grey-level value $N$ on the density profile

However, in the above model one must take into account the background variation (Swanson et al, 1983; Tobis et al, 1983), whose principal effect is to alter the degree of greying between the two extreme points, A and B, at the base of the density profile (Fig 5). In the first approximation, we have assumed that along a length of a slice the variation in brightness of the background between points A and B is linear. Subsequently, if we cancel background pixel values, we obtain a new value, $N'$, for each intervening pixel (*e.g.* point M), such that.

$$N' = N - N_b \qquad (2)$$

where $N$ is the raw value of the pixel M, and $N_b$ its background value. Background correction was applied in this way for all pixels along the length of a section between the extreme points, A and B, located at the shoulder of the density profile. In fact, as we have considered that the volume was represented by a series of sections, the line joining all points A and B of all density profiles corresponded to the LV contour

The determination of this contour was then made in two steps (Fig. 5): (1) choice of a threshold using a false colour display on the video monitor, that allowed us to

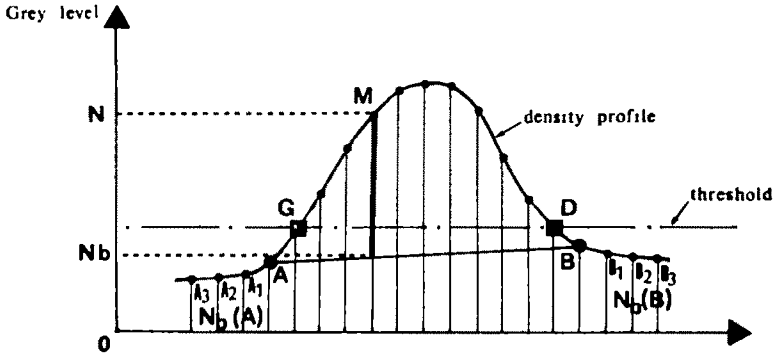

FIG. 5

Diagram of a density profile showing how the boundaries of points A and B were determined, and the value $N'$ of the background.

find the co-ordinates G and D corresponding to a visual approximation of the opacified contour cavity, and (2) use of an automatic contour detector (sobel operator) which permitted us to measure the brightness gradients in the vicinity of the co-ordinates G and D During this operation, when the slope alterations of the density profile became very small we assumed that this area corresponded to the projection of points A and B (*i.e.* the points included in the real edge of the contour). Values of the background were then calculated on both shoulders of each density profile by averaging the three pixel values next to the points A and B, such that:

$$N_b(\mathrm{A}) = N_{\mathrm{A}_1} + N_{\mathrm{A}_2} + N_{\mathrm{A}_3}$$

and

$$N_b(\mathrm{B}) = N_{\mathrm{B}_1} + N_{\mathrm{B}_2} + N_{\mathrm{B}_3}$$

Moreover, this process enabled the operator to choose freely the direction of the sections, without having to worry about their relationship to the long axis of the ventricle. In practical terms, the operator visually locates the plane of the aortic valve after selecting the two most distant points in this plane in an interactive manner; the direction of the cuts is then automatically drawn parallel to this plane (Fig. 6).

The end-diastolic volume (EDV) and end-systolic volume (ESV) are obtained using the following formulae

$$\mathrm{EDV} = k\left[\sum_{(c)} N'i\right] S_\mathrm{E}\Delta\mu \qquad (3a)$$

$$\mathrm{ESV} = k\left[\sum_{(c')} N'j\right] S'_\mathrm{E}\Delta\mu' \qquad (3b)$$

where $k$ = geometrical constant, ($c$) and ($c'$) = projected areas of EDV and ESV, $S_\mathrm{E}$ and $S'_\mathrm{E}$ = elementary area of ($c$) and ($c'$), and $\Delta\mu$ and $\Delta\mu'$ = proportionality constants related to linear attenuation coefficients.

Furthermore, because of the intravenous injection, we assumed that during a cardiac cycle neither the concentration of contrast medium in the ventricular cavity nor the X-ray energy varied, resulting in equality of the proportionality constants, such that $\Delta\mu = \Delta\mu'$.

Therefore, the computation of LV ejection fraction (EF) is obtained from:

$$\mathrm{EF} = \frac{\mathrm{EDV}-\mathrm{ESV}}{\mathrm{EDV}} = \frac{(\mathrm{EDV}/\mathrm{ESV})-1}{\mathrm{EDV}/\mathrm{ESV}} \qquad (4)$$

where $k$ and $\Delta\mu$ have been cancelled in the fraction for the reasons stated above.

During the time required for the calculations the density profiles of each section could be simultaneously viewed on a video monitor.

## RESULTS

### *Experimental protocol*

For the first group of three phantoms with 5% iodine concentration we compared the real results of the simulated EF to those calculated by geometric and videodensitometric methods (Table I) The discrepancy in the results for Case 3 was probably due to the distortion of the balloon

For the second group of six phantoms with different iodine concentrations, we compared the values of the real volume injected and the simulated EF with those calculated by videodensitometric analysis (Table II).

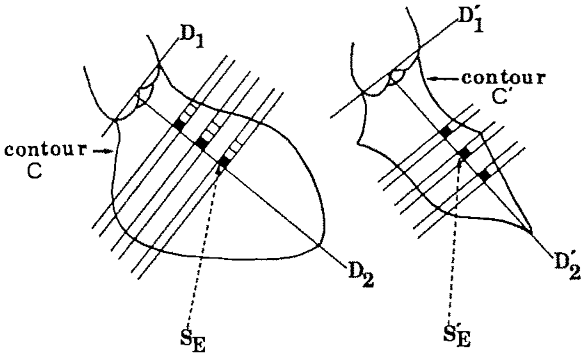

FIG. 6

Determination of the cross-sectional area of the left ventricle. The operator determines the aortic planes $D_1$ (EDI) and $D'_1$ (ESI) on the video monitor Further planes are then automatically drawn parallel to $D_1$ or $D'_1$

TABLE I

COMPARISON OF EF MEASUREMENTS OBTAINED BY GEOMETRIC ANALYSIS AND BY VIDEODENSITOMETRIC ANALYSIS FOR THREE FLUID-FILLED BALLOONS

| Case | EDV (cm$^3$) | ESV (cm$^3$) | SEF | Calculated EF | |
|---|---|---|---|---|---|
| | | | | Geometric analysis | Videodensitometric analysis |
| 1 | 160 | 40 | 0.75 | 0.78 | 0.73 |
| 2 | 130 | 30 | 0.76 | 0.746 | 0.74 |
| 3 | 80 | 40 | 0 50 | 0.678 | 0 52 |

Contrast medium iodine concentration 5%.
SEF = simulated ejection fraction

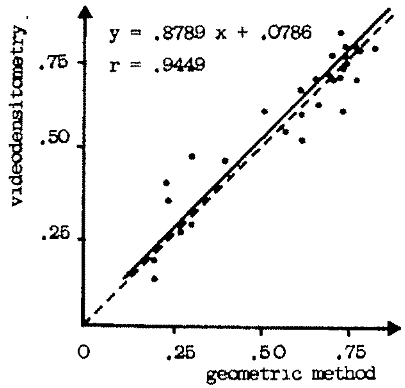

FIG 7

Comparison of the ejection fraction results obtained by geometric methods and by videodensitometric analysis.

*Clinical protocol*

The results of measurements obtained by videodensitometry and by the geometric method were compared and, from these values, the correlation coefficient as well as the regression equation were calculated (Fig. 7). The results showed a good correlation coefficient ($r = 0.9449$ with $y = 0.8789, x + 0.0786$).

DISCUSSION

Digital left ventriculography by the intravenous or direct approach has now proved its value for studying LV function (Nichols et al, 1983; Tobis et al, 1983; Detrano et al, 1985) and degree of stenosis (Serruys et al, 1984; Simons & Kruger, 1985). However, most of the previous attempts to quantify LV volumes were based on geometric methods. Subsequently, digital videodensitometry was introduced as a different technique of absorption densitometry which utilises processing of a digital subtracted image (Tobis et al, 1983; Greenbaum & Evans, 1984; Detrano et al, 1985), allowing geometric assumptions for the ventricle to be disregarded.

Many factors have to be considered in evaluation of videodensitometric measurements. One of these is the mode of X-ray emission, which affects the X-ray intensity received by the image intensifier. Since the quantity of information contained in an image depends on the number of photons received by the detector, the use of an X-ray emission with a higher mA is required to produce a good-quality image. This technical condition was provided by seriographic or pulsed acquisition mode which worked on our equipment. This type of X-ray emission provides a lower level of background noise than that of the continuous mode, and allows improved measurement of pixel brightness around the silhouette of the area of interest.

With our process the automatic determination of the LV contour provides more accurate results of volume measurements than those obtained by manual determination of the contour, or the use of the threshold technique alone undertaken by some workers (Tobis et al, 1983; Greenbaum & Evans, 1984). Thus, for the determination of LV volume and ejection fraction, the plane direction of a cross-sectional area did not intervene in the calculation of the ventricular volume,

TABLE II

VOLUME MEASUREMENT BY VIDEODENSITOMETRIC ANALYSIS OF SIX BALLOONS FILLED WITH CONTRAST MEDIUM OF DIFFERENT IODINE CONCENTRATIONS

| Case | CMC (%) | Real volumes injected | | | Volume values obtained by videodensitometry | | |
|---|---|---|---|---|---|---|---|
| | | DV (cm$^3$) | SV (cm$^3$) | SEF | DV (cm$^3$) | SV (cm$^3$) | SEF |
| 4 | 5 | 100 | 50 | 0.5 | 115 | 52 | 0 45 |
| 5 | 5 | 159 | 79 | 0.5 | 155 | 82 | 0 47 |
| 6 | 3 | 100 | 50 | 0.5 | 105 | 47 | 0.44 |
| 7 | 3 | 91 | 31 | 0.67 | 86.6 | 32.4 | 0 62 |
| 8 | 2 | 100 | 50 | 0.5 | 110 5 | 49.8 | 0.45 |
| 9 | 2 | 121 | 61 | 0.5 | 118 | 57 3 | 0.45 |

CMC = contrast medium iodine concentration, DV = diastolic volume, SV = systolic volume, SEF = simulated ejection fraction

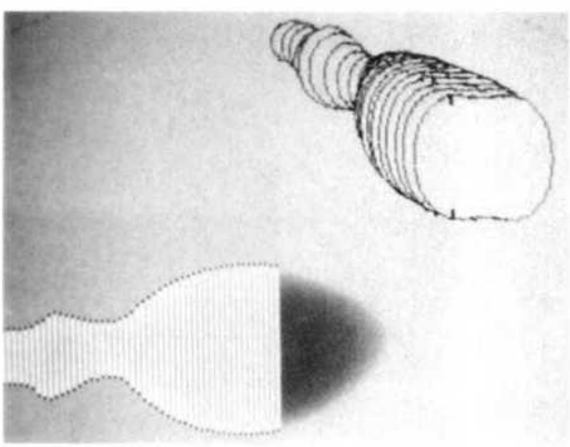

FIG. 8.

Display of density profiles automatically drawn on the projected area of a fluid-filled balloon and three-dimensional perspective of the balloon volume.

since a change in the direction only resulted in the change in the elementary area ($S_E$) which, in turn, represented the multiplier coefficient of the sum of pixel values depicting the interior of the contour.

Some other factors have to be taken into account in clinical applications of measurements of the ventricular cavity: (1) geometric distortion inherent in the image intensifier, (2) fluctuations in X-ray output over time, (3) spatial variation in the intensity of the X-ray beam, (4) X-ray scatter and veiling glare, and (5) variation in the degree of opacification of the periventricular region resulting from the opacification of the background of the region of interest.

In practice, we disregarded the geometric distortion by working in the centre of the image intensifier field, and we checked the linearity of the X-ray chain, but we did not make attempts to correct X-ray scatter or veiling glare, as proposed by Shaw et al (1982).

In fact, as emphasised by most workers, the most important factor which interferes with videodensitometric results seems to be the background variation in relation to tissue iodine accumulation (Swanson et al, 1983; Tobis et al, 1983). As we have already pointed out, in our method, background variations in the periventricular region are taken into account separately on each selected image for the computation of pixel values, *i.e.* on the opacified subtraction image (EDI and ESI). The choice of the same image for the calculation of pixel values of the area of interest and of background allows the cancellation of temporal emission fluctuations of the X-ray source. Moreover, to account precisely for the variation in background opacification in the neighbouring tissues, background correction was performed pixel by pixel on each section of the volume. This technique obviously provides superior results to the overall background correction employed by Tobis et al (1983). In fact, with the latter method, only a mean level of opacification can be calculated in an area included in the manually outlined systolic and diastolic contours.

As already noted, our process allows free choice of the direction of the cut plane. According to the direction of slice chosen by the operator, the density profiles are displayed on the monitor, which provides a visual display of the geometric shape of the fluid-filled balloon or of the ventricle (Fig. 8). This provides information about the third dimension of the ventricle, which will probably be of interest when the program is applied to an aneurysmal cavity.

## CONCLUSION

As we have shown previously (Sandor et al, 1979), DSA is a relatively simple and convenient way of visualising the left ventricle and determining ejection fraction by geometric methods. In this paper, we have demonstrated that the digital videodensitometric method can be applied to digital angiograms obtained following intravenous injection of contrast medium, and that the accuracy of the results could be superior to those obtained by geometric methods.

Finally, even though all of the patients in this series had a ventricular cavity without deformity, we believe that videodensitometry will be helpful for investigation of aneurysmal cavities.

## ACKNOWLEDGMENTS

This work was supported by the "Institut National de la Santé et de la Recherche Médicale" (INSERM) and the "Caisse Nationale d'Assurance Maladie des Travailleurs Salariés (CNAMTS). Ph. Brenot was supported by a training grant from the "Fonds d'Etudes du Corps Médical des Hôpitaux de Paris".

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# Book reviews

*Noninvasive Diagnostic Techniques in Vascular Disease,* 3rd edit. Ed by Eugene F. Bernstein, pp. xvii+918, 1985 (Blackwell Scientific Publications, Oxford), £95 00
ISBN 0–8016–0596–2

This book is the third edition, the first appeared in 1978 and the second in 1982 However, it is a much larger review of non-invasive diagnostic techniques in vascular disease than either of the previous editions. In his preface to the present volume, Dr Eugene Bernstein points out that approximately 50 of the 87 chapters are new or are radical revisions.

The book is divided into three major sections, the first, "Fundamentals of measurement and current instrumentation", contains 27 chapters, the second, "Area of application. detection, quantitation, and prediction", contains 58 contributions, the third, "Practical aspects", contains two chapters concerned with the organisation of a vascular laboratory In the first of these major sections there are subsections dealing with· velocity measurement using Doppler ultrasound; pressure measurement; volume measurement using plethysmographic techniques, radionuclide techniques, and vascular imaging, using ultrasound, digital subtraction angiography, positron emission tomography, and magnetic resonance imaging. These contributions combine to produce a well balanced and well presented review of all the major techniques and instrumentation for studying blood vessels

In the second major section there are contributions dealing with extracranial occlusive disease, with a discussion of indirect tests such as oculo- and oculopneumoplethysmography and direct tests such as phonoangiography, various Doppler ultrasound methods and digital subtraction angiography Peripheral arterial disease also has a large subsection. Pressure measurements, radionuclide techniques and ultrasound duplex scanning are described in detail. This is followed by a major subsection on peripheral venous disease, and the parts Doppler ultrasound, plethysmography, radioactive fibrinogen, and thermography play in the diagnosis

This book is well produced and achieves its aim of presenting the state of the art in non-invasive diagnostic techniques It is a very good overall review and deserves to find a place on the bookshelves of all self-respecting departments of radiology and surgery.

J P WOODCOCK

*Basic Imaging in Congenital Heart Disease,* 3rd edit By Leonard E. Swischuk and David W. Sapire, pp xiv+312, 1986 (Williams & Wilkins, Baltimore), £55.00.
ISBN 0–683–08055–5

Publication of a further edition indicates the success of this work, which was originally devoted to the interpretation of plain radiographs. The main addition to this third edition is cardiac ultrasonography As before, detailed angiocardiography is omitted and as nuclear medicine imaging in the author's institution is used primarily for myocardial scanning, this is not considered either Similarly, the place of magnetic resonance imaging (MRI) is unlikely to replace current investigative procedures and so is also omitted from this edition

Embryological development of the heart and fetal circulation are described and then normal anatomy is illustrated from plain radiographs, angiocardiograms and MRI scans Physiological considerations in congenital heart disease are discussed, as is pulmonary hypertension Chapter 2 is an extensive exposition of the evaluation of the plain radiograph, encompassing basic pulmonary vasculature, the cardiac silhouette and the various ancillary findings. Chapter 3 is a clear and succinct review of both M-mode and two-dimensional echocardiography The fourth chapter, which makes up most of the book, is a classification of congenital heart disease, essentially based on pulmonary vascular patterns Each defect is well considered with clinical, haemodynamic, plain radiograph, ultrasound and angiographic findings well displayed. The last chapter is composite, dealing with cardiac malpositions, vascular anomalies and the special problems in neonates and also in adults, with whom this treatise is generally not concerned. The final section consists of some illustrative case reports

The book, as before, is comprehensive, well illustrated, clear and easy to understand Few radiologists are likely to have the opportunity to practise neonatal cardio-angiography, but this remains an excellent exposition of the plain radiographs which any practising radiologist may encounter The new chapter on echocardiography is pleasingly clear and informative

D G. SHAW

1987, *The British Journal of Radiology*, 60, 701–702

# Case reports

## Magnetic resonance imaging of syringomyelia occurring after operation on spinal intramedullary tumours by Cavitron ultrasonic aspirator

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*(Received November 1986 and in revised form February 1987)*

Conservative therapy, such as irradiation of spinal-cord tumours, is commonly associated with progressive neurological deterioration. It has been claimed that radical excision of such tumours with the Cavitron ultrasonic aspiration (CUSA) technique may be achieved without any, or with minimal, neurological sequelae (Epstein & Epstein, 1981, 1982a; Epstein, 1983). This technique apparently enables gross total removal of astrocytomas and ependymomas of the spinal cord with essentially no retraction of adjacent tissue. Patients with mild to moderate neurological deficits have been observed who showed dramatic clinical improvement after operation with the CUSA technique (Flamm et al, 1978; Epstein & Epstein, 1981, 1982b).

### CASE REPORTS

*Case 1*

A 12-year-old boy complained of progressive difficulty in walking. On examination, he had mild quadriparesis with diminished jerks in both arms, brisk reflexes in both legs, and bilateral Babinski signs. There was no sensory deficit and the patient was continent. Myelography showed a block at the C6 vertebral level. Magnetic resonance imaging (MRI) demonstrated diffuse widening of the spinal cord from C1 to T2 with no cysts (Fig. 1). An intramedullary astrocytoma extending

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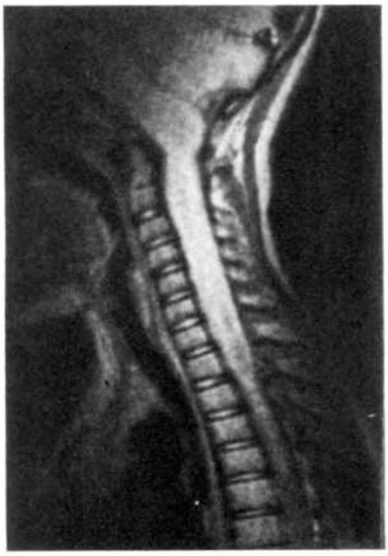

FIG. 1. *Case 1.*

An MRI scan before surgery (time to repeat (TR) = 2000 ms, time to echo (TE) = 50 ms). Diffuse widening of the spinal cord, demonstrated with higher signal from C1 to T2. The finding corresponded with an intramedullary tumour.

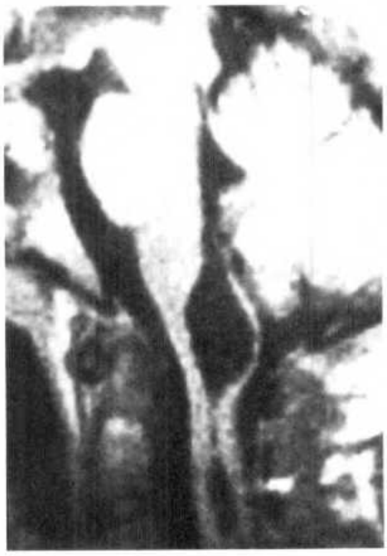

FIG. 2. *Case 1.*

An MRI scan 4 months after surgery (TR = 500 ms, TE = 50 ms). Two cystic dilatations of the spinal cord are seen, one at the level of C1 and the other at the level of C2–C3. Note the pressure on the medulla oblongata (syringobulbia).

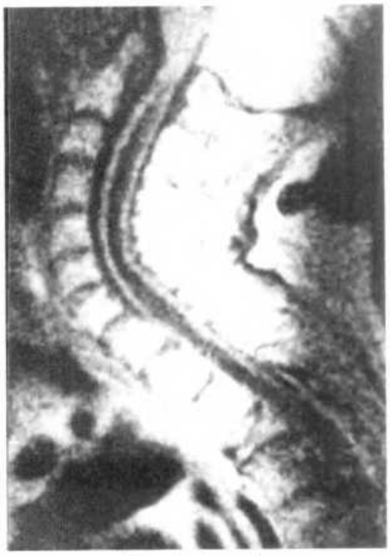

FIG. 3. *Case 2.*

An MRI scan (TR = 600 ms, TE = 50 ms) of the cervical and upper thoracic spine 5 months after surgery showing a syrinx in the cervical and upper thoracic spinal cord.

1987, *The British Journal of Radiology*, *60*, 702–704

from C1 to T2 was removed in its entirety using the CUSA technique

For 5 months after surgery, the patient's gait improved, but deteriorated thereafter. Examination revealed a spastic lower paraparesis and flaccid weakness of the upper extremities Hypoaesthesia was present in the distribution of all segments, including the trigeminal nerve bilaterally and fasciculation of the tongue was observed

Repeat MRI showed two cystic dilatations of the spinal cord, one at the level of the foramen magnum and one at the level of the C2 and C3 vertebrae (Fig 2)

*Case 2*

A 17-year-old man complained of progressive weakness in his legs On neurological examination, a mild spastic paraparesis and hypoaesthesia below T10 were found. There was no disturbance of micturition. Ascending myelography demonstrated a block at the level of T9 and suboccipital injection also showed a block at the level of C6 An intramedullary ependymoma was removed by the CUSA technique The patient improved dramatically post-operatively, but 5 months later his gait deteriorated. An MRI scan demonstrated syringomyelia (Fig. 3).

## DISCUSSION

Removal of spinal intramedullary astrocytomas and ependymomas by CUSA with or without laser technique seems at present to be the procedure of choice These tumours are usually soft and it is claimed that the CUSA technique enables complete removal without retraction of the underlying spinal-cord tissue (Epstein & Epstein, 1981, 1982a, b; Flamm et al, 1978).

The reported improvement in clinical signs and symptoms after surgery is evidence of the advantages of this procedure but syringomyelia or syringobulbia after surgery with the CUSA technique has, to the best of our knowledge, not yet been reported. In our cases, the computed tomographic and MRI scans did not show any tumour cysts or cavitations before surgery The syrinxes therefore developed post-operatively.

As in primary syringomyelia, it is not known why the cerebrospinal fluid enters the syrinx but is unable to leave it while a communication exists with the subarachnoid space. Such a combination may exist with the fourth ventricle through a patent central canal or via the Virchow-Robin spaces around penetrating arteries. Shunt procedures may, in certain cases, reduce the size of the syrinx and alleviate clinical signs and symptoms (Pearless & Durward, 1982).

It is therefore imperative that syrinx formation after CUSA surgery of the spinal cord be kept in mind in cases of deterioration of neurological symptoms after a lucid interval. Magnetic resonance imaging is then the diagnostic procedure of choice.

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# Neuropathic arthropathy as a complication of post-traumatic syringomyelia

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The causes of neuropathic arthropathy, also called Charcot joints, are well known. They include developmental syringomyelia, myelomeningocele, diabetes mellitus, peripheral nerve injuries, syphilis, leprosy, congenital insensitivity to pain and acrodystrophic neuropathy (Banna & Foster, 1972).

The purpose of this communication is to add post-traumatic syringomyelia as another possible cause of Charcot's arthropathy.

## CASE REPORT

A 50-year-old man was admitted to King Khalid University Hospital with a 2-week history of fever and painless swelling of the right shoulder Five months earlier, he had presented with the same symptoms at a different hospital, where a diagnosis of infective arthritis was made and the joint was drained

Seventeen years previously, the patient had sustained a compression fracture of the first lumbar vertebra when a heavy object fell on his back He became paralysed below the level of the injury but gradually improved following surgical

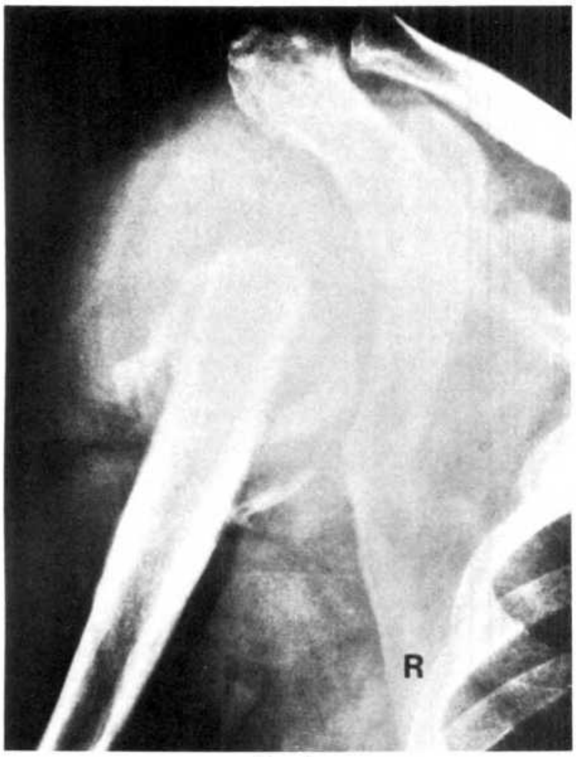

FIG. 1.

Neuropathic right shoulder joint. There is severe destruction and extensive disorganisation of the right shoulder which was swollen and painless. Similar changes were present on the left side.

decompression and was finally able to walk aided with a stick.

On examination the patient was found to be pale and febrile (temperature 39.3°C) with tachycardia. His blood pressure was normal and he was mildly diabetic. His right shoulder was swollen, red and hot with dilated superficial veins, but there was no pain.

Neurological examination of the upper limbs revealed a claw left hand, atrophic ulcers over the knuckles and atrophy of the small muscles of both hands. Motor power in both upper limbs was decreased and muscle reflexes were absent. He had dissociated sensory loss for pain and temperature involving the upper limbs and the upper part of the chest. Both lower limbs were weak and there was muscle wasting but the tendon reflexes were intact. There was impaired sensation to all modalities in both legs.

Numerous laboratory tests were non-contributory. These included tuberculin test, Paul Bunnel and brucellosis antibody tests, and VDRL. Blood culture showed haemolytic *Streptococcus* and *Staphylococcus aureus*. Joint aspirate culture showed no bacterial growth.

Spine radiographs revealed an old compression fracture of L1 with significant narrowing of the D12–L1 disc space. Both shoulder joints showed extensive bone destruction associated with effusion and disorganisation indicative of neuropathic joints (Fig. 1). A lumbar-route myelogram showed complete block at D12 and computed tomography (CT) performed following the myelogram and also 6 and 12 h later showed an enlarged spinal cord with opacification of a syrinx on the delayed study. The syrinx extended the entire length of the spinal cord to the level of the atlas (Fig. 2).

## DISCUSSION

Post-traumatic syringomyelia is a rare but exceedingly important complication of spinal injuries. It was first described by Strumpell in 1880. It occurs in

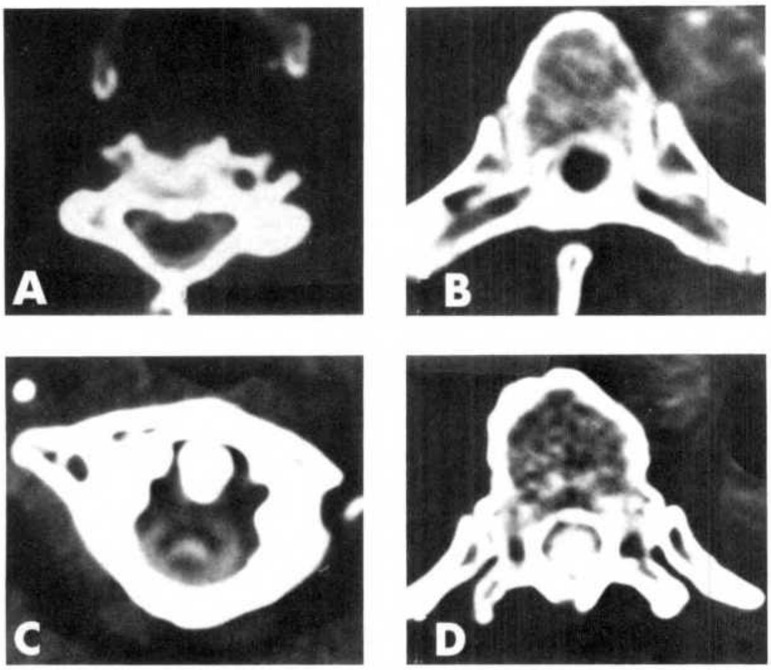

FIG. 2.

CT myelogram (A–D). (A) and (B) are CT sections in the cervical and thoracic spine, showing expansion of the spinal cord. (C) and (D) are delayed CT sections obtained 12 h following the introduction of the contrast medium, showing opacification of the syrinx.

approximately 0.5–1.9% of spinal injuries (Barnett & Jousse, 1973) and unless recognised early and properly treated, can render a paraplegic patient into a helpless, severely handicapped quadriplegic With the increasing availability of CT and magnetic resonance imaging the incidence of this complication could be found to be higher than previously reported. Early diagnosis and proper treatment halts further deterioration and often improves the neurological deficit. The case which is presented shows that untreated post-traumatic syringomyelia can cause an incapacitating arthropathy in addition to progressive neuropathy.

In post-traumatic syringomyelia, the relationship between the severity of the injury and the onset of symptoms varies from case to case Whilst Barnett and Jousse (1973) found that symptoms from the cyst appeared more rapidly in the severely injured patient, others found no relationship between the severity of the injury and the onset of symptoms (Quencer et al, 1983). In this latter study of 16 patients with post-traumatic spinal-cord cysts, the duration of injury varied from 3 months to 13 years.

Neuropathic joint is a known late complication of developmental syringomyelia, but it is rare for patients with this type of syringomyelia to present with arthropathy. However, very few cases of post-traumatic syringomyelia presenting with neuropathic joints have been reported (Walbom-Jorgensen, 1966; Sackellares & Swift, 1976, Rhoades et al, 1983).

The pathogenesis of post-traumatic syringomyelia is uncertain. It is believed that trauma causes a core of myelomalacia (softening) of the spinal cord, with subsequent necrosis and cavitation. Further extension of the lesion has been attributed to a number of factors which include local ischaemia (Turnball et al, 1966), the action of released lysosomes (Kao & Chang, 1977), increased levels of epinephrine-like substances with consequent vasoconstrictor effect, and to increased cavitary fluid and pressure changes transmitted from the subarachnoid space (Osterholm & Mathews, 1972). Increased hydrostatic pressure caused by straining and Valsalva manoeuvres extend the syrinx cranially, while the pressure gradient across a block in the subarachnoid space promotes a caudal extension of the syrinx The caudal extension leads to further neural damage, but the caudal extension may not be apparent clinically unless the patient has been only partially paralysed at the time of the injury.

Syringomyelia is easily detectable by magnetic resonance imaging. Where this modality is not available, the findings at water-soluble CT myelography are equally diagnostic. An early CT scan performed immediately following the myelogram will show an expanded cord but may or may not reveal the syrinx. The syrinx may be opacified on scans performed 3, 6, 12 or even 24 h following the intrathecal contrast injection (Banna, 1985).

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1987, *The British Journal of Radiology*, 60, 705–706 JULY 1987

*Case reports*

# Congenital bilateral glenoid hypoplasia: a report of four cases

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(*Received June 1986 and in revised form September 1986*)

Congenital bilateral glenoid hypoplasia was regarded as a rare anomaly until recently (Laurent, 1958; Moser, 1958; Triquet et al, 1980; Resnick et al, 1982). Petterson (1981) found 20 cases in the literature and added nine of his own. Kozlowski et al (1985) reported this anomaly in eight patients, including six children. Since that time we have found four further cases and these are now described.

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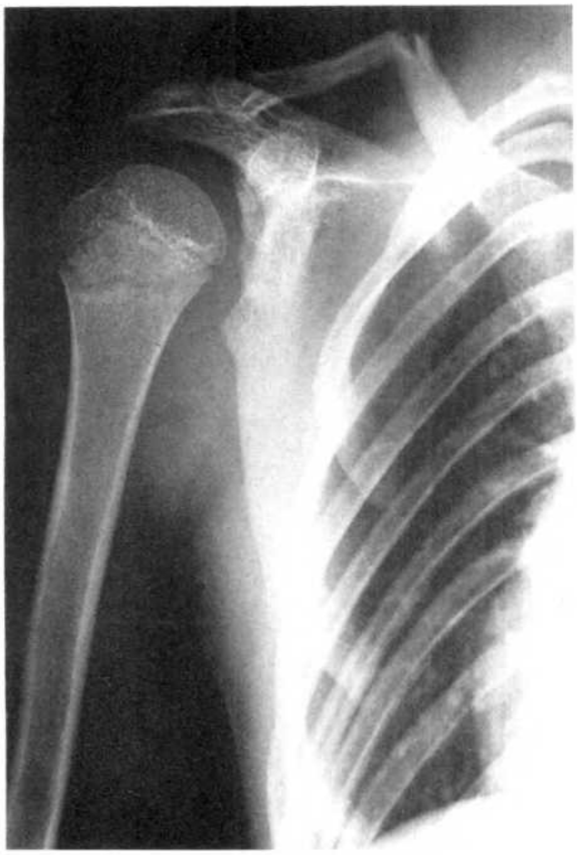

FIG. 1. *Case 1.*
The glenoid fossae are shallow and irregular. The acromion is prominent.

## CASE REPORTS

### *Case 1*

An 8-year-old boy had previously been treated for congenital dislocation of the left hip. A chest radiograph at that time showed bilateral glenoid hypoplasia. He was seen again at the age of 8 years because of a fractured clavicle (Fig. 1). The boy is otherwise well, has normal height and has no functional disability in his shoulders. Skin dimples were present posteriorly on both sides at the level of acromion.

### *Case 2*

This patient, the father of the patient in Case 1, has occasional pain in his shoulders but no disability. Radiographic examination showed bilateral glenoid hypoplasia (Fig. 2). His hips were radiographically normal. He had shoulder skin dimples similar to his son.

### *Case 3*

In this 8-year-old boy bilateral glenoid hypoplasia was discovered accidentally when a skeletal survey (Fig. 3) was performed after a road accident.

### *Case 4*

Bilateral glenoid hypoplasia was discovered incidently during a skeletal survey in this socially neglected 13-month-old girl (Fig. 4).

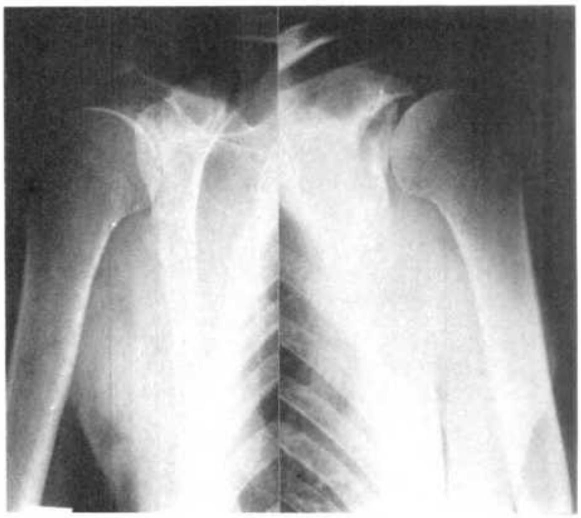

FIG. 2. *Case 2.*
Radiograph showing bilateral glenoid hypoplasia.

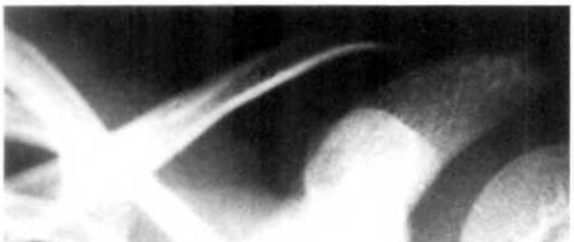

FIG. 3. *Case 3.*

The glenoid fossae are shallow and irregular. The acromion is prominent.

## DISCUSSION

Isolated bilateral glenoid hypoplasia in children is a rarely recognised congenital anomaly which causes little if any disability. However, adult patients with this malformation may be susceptible to recurrent shoulder pain, dislocations and early osteoarthritic change. They should therefore avoid circumstances which put undue strain on the shoulder joints, particularly certain sports, such as tennis, javelin and all contact sports.

In cases of glenoid hypoplasia, osteochondrodystrophies, specifically spondylo-epiphyseal, spondylo-metaphyseal and metaphyseal dysplasias should be excluded. One of our cases had congenital dislocation of his left hip and perhaps an association also exists with this condition.

Dominant inheritance of glenoid hypoplasia has been proven. Petterson (1981) has reported the disease in a father and daughter. In our 12 patients, two families showed a dominant type of inheritance (father and son, and a mother and two siblings). However, in most sporadic cases familial studies have not been performed. These cases may still represent either a recessive mode of inheritance or new dominant mutations.

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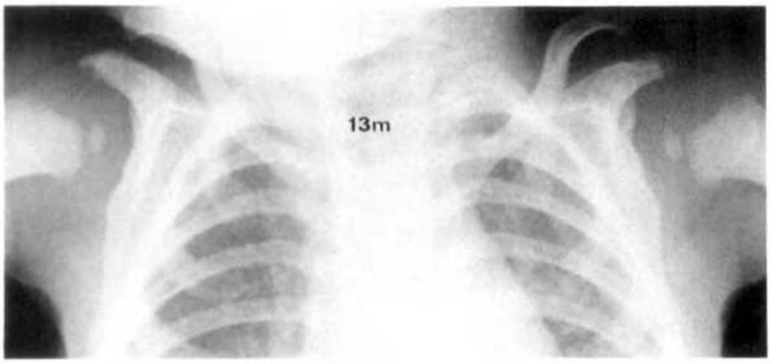

FIG. 4. *Case 4.*

The glenoid fossae are shallow and irregular.

1987, *The British Journal of Radiology*, 60, 707–710 JULY 1987

*Case reports*

# Metaphyseal dyschondroplasia with cone-shaped epiphyses

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*(Received July 1986 and in revised form October 1986)*

A case of metaphyseal dyschondroplasia is reported with the unusual feature of cone-shaped epiphyses of the tibiae and bones of the hand.

## CASE REPORT

An 8-year-old boy (born June 1972) was admitted in 1980 having had bowed lower limbs since the age of 4 years. The child showed reduction in stature and weight but had normal mental development. The limbs and hands were short compared with the trunk. No visceral abnormality or alopecia was present. The bilateral genu varum and genu recurvatum were considered to be secondary to the abnormal length of both fibulae. Consequently, bilateral fibular resection was performed in December 1980 and the genu varum became stabilised. We saw the child for the first time in October 1984, when dwarfism was marked. His height was 1.08 m (−7 SD) and his weight was 21.95 kg (−3 SD) at an age of 12 years and 4 months. At birth his weight had been 2.95 kg and he measured 47 cm in length. He had suffered from no significant disease during childhood and, in particular, had not had meningococcal septicaemia. He showed no mental retardation and performed well at school. His parents are unrelated; the mother is 1.5 m tall, father 1.68 m. Three siblings, aged 11, 9 and 3 years, have normal stature.

Radiographs of the boy obtained in 1980 and 1984 show similar findings. The skull shows normal craniofacial relationships. The spine (Fig. 1) shows some minimal irregularities of the vertebral end-plates and some reduction in height of the posterior part of the vertebral bodies. No abnormality was demonstrated in the thoracic spine.

The principal anomalies in the long bones are metaphyseal. In the proximal humerus (Fig. 2), marked metaphyseal changes are shown in the medial half of the metaphysis, which is irregular and flattened with an associated varus deformity of the humeral head. In the lower limb, the femoral head is normal (Fig. 3) but there is premature fusion of the proximal growth-plate. The lateral half of the metaphyseal region shows some increased density and slight coxa vara is present. The distal femur, including the metaphysis, shows no abnormality. The proximal metaphysis of the tibia is irregular and cupped with some evidence of a cone epiphysis. Considerable overgrowth of the fibula is present on both sides (Fig. 4) and both genu varum and genu recurvatum are present. Metaphyseal changes affect the distal ends of both tibiae and fibulae, although coned epiphyses are not observed in the fibulae.

In the feet, premature fusion of the metatarsal and phalangeal epiphyses had occurred; this normally does not take place before the age of 15 years. The bones of the hands are very abnormal (Fig. 5) with marked coning of the epiphyses of the metacarpals and the second, third, fourth and fifth middle phalanges uniformly on both sides. The terminal tufts are hypoplastic but no coning is evident in the proximal or distal phalanges. The metaphyses of the proximal phalanges are, however, not normal. All the metacarpals are short. In the thumb the metacarpal is slightly short with greater shortening of the proximal phalanx, but the terminal tuft is relatively normal. No significant changes are present in the distal metaphyses of the radius and ulna.

Bone age is difficult to assess on the radiographs of the hand from 1984 because of inconsistencies in the various segments.

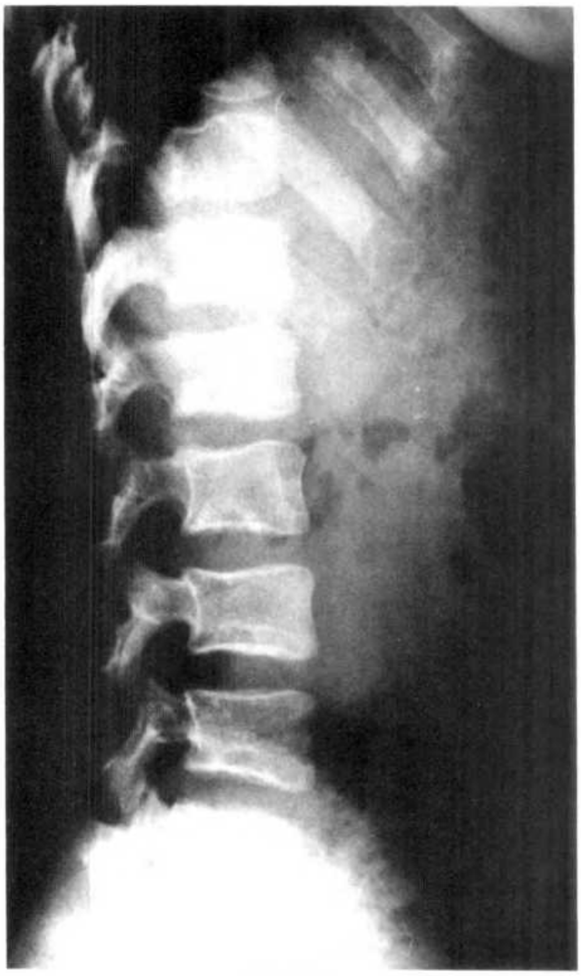

FIG. 1.

Lateral view of the spine, showing minimal irregularity and narrowing in the posterior portion of the body, with evidence of Schmorl's disease.

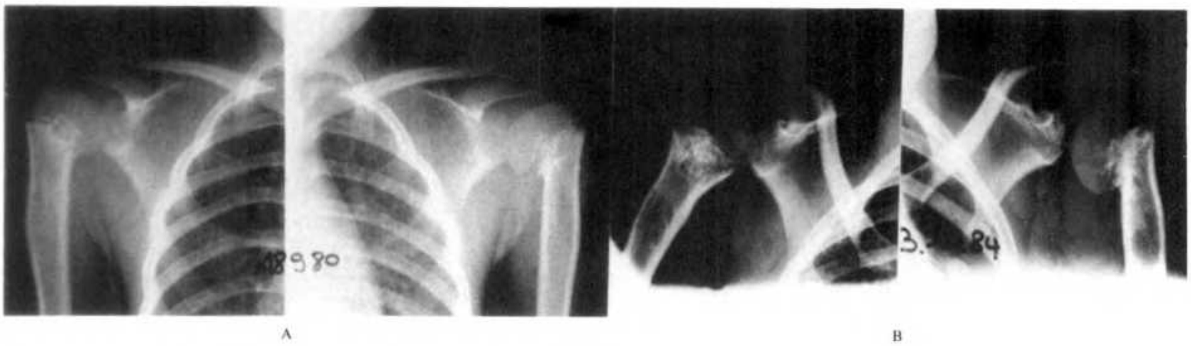

FIG. 2.

Radiographs of the shoulder: frontal view at (A) 8 years old and (B) 12 years old. Proximal humerus shows marked metaphyseal changes with a varus deformity, especially on the left side.

No sesamoid bones are identifiable. From assessment of the carpal centres and the distal radius and ulna, the bone age seems to be approximately 10 years. However, were the metacarpals and phalanges to be assessed, the bone age could be said to lie between 15 years and 16 years. Overall, the bone age appears to be advanced, with premature fusion of many growth-plates, particularly in the femur and hands.

Skeletal radiographs of the patient's mother and father (hands, hips and knees) were normal.

The conclusion from the radiographic examination is that this is a metaphyseal dyschondroplasia involving mainly the humeri, tibiae, fibulae, metacarpals and digits, with cone epiphyses in certain areas.

## DISCUSSION

Although this case shows evidence of a metaphyseal dyschondroplasia, certain features are not at all typical of the type described by Schmid (Maroteaux, 1982; Beluffi et al, 1983). These features include cone epiphyses, overgrowth of the fibula and brachydactyly. The occurrence of cone-shaped epiphyses is observed in many bone diseases (Table I) and, indeed, such changes in the distal phalanx of the thumb and the middle phalanx of the little finger, as well as the middle finger, can constitute a normal variant (Giedion, 1965). The changes are, however, always abnormal when occurring in the middle phalanx of the second to fifth rays and are very unusual in the proximal tibia.

Cone-shaped epiphyses of the hands with brachydactyly can be observed in the rhino-tricho-phalangeal syndrome (Giedion, 1965), but here brachydactylia is not uniform as in our case and no metaphyseal changes are present. Cone-shaped epiphyses are not a feature of

TABLE I

DISEASES WITH CONE-SHAPED EPIPHYSIS

(i) Congenital diseases
  Ellis Van Creveld syndrome
  Cleidocranial dysostosis
  Acrodysplasia:
    Brailsford peripheral dysostosis
    Tricho-rhino-phalangeal syndrome
    Acrodysostosis
  Achondroplasia and hypochondroplasia
  Asphyxiating thoracic dystrophy
  Otofaciodigital syndrome
  Otopalatodigital syndrome
  Hand-foot-uterus syndrome
  Frontometaphyseal dysplasia
  Saldino and Mainzer syndrome
  Beckwith-Wiedemann syndrome
  Kaschin-Beck disease
  Marchesani syndrome
  Phalangeal gigantism
  Thiemann disease
  Giedion-Langer syndrome
  Pseudohypoparathyroidism
  Familial metaphyseal dysplasia
  Clinodactyly
  Trisomy 21
  Turner's syndrome
  Klinefelter's syndrome
  Steinert disease
  Cornelia de Lange syndrome
  Larsen's syndrome
  Apert's syndrome or acrocephalopolysyndactyly
  Pseudohypoparathyroidism
  Neonatal hyperparathyroidism
  Osteopetrosis
  Parastremmatic dwarfism
  Hemimelic epiphyseal dysplasia
  Dyggve-Melchior-Clausen syndrome
  Anorchidia
  Hypopituitarism

(ii) Acquired diseases
  Rickets
  Trauma
  Infection
  Bone infarcts
  Sickle-cell disease
  Frostbite
  Hypervitaminosis A

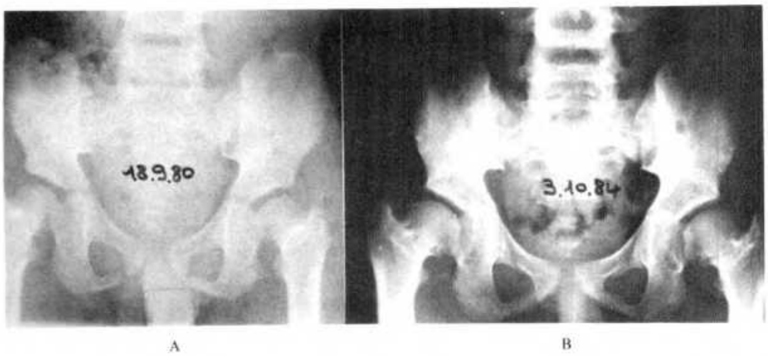

FIG. 3.

Frontal view of the pelvis at (A) 8 years old and (B) 12 years old. The proximal femur shows no significant abnormality although fusion has already occurred. The acetabula are oblique and there may be a slight degree of subluxation of the femoral heads.

metaphyseal dyschondroplasia as described by Schmid. Metaphyseal changes of the type shown in our case may be present in hypochondroplasia (Hall & Spranger, 1979), where the distal fibula may be lengthened. However, coned epiphyses are not observed and the pelvis is small in addition to the abnormal reduction in the lumbar interpediculate distances. Cartilage-hair hypoplasia syndrome (McKusick et al, 1965) might be considered in terms of the bony changes but in our case no abnormality of the hair was present and the distal femur was normal. Review of the literature shows that some cases bear a resemblance to our patient but none is identical. Jequier et al (1981) and Bellini (1966) report two cases of metaphyseal dyschondroplasia with ectodermal dysplasia in Italian patients. Their first case had marked cupping of the metaphyses and cone epiphyses combined with complete alopecia. The second, identical case was found in another Italian patient. In both cases the metaphysis was cupped with a cone epiphysis within it in the long tubular bones, hands and feet. In addition, spinal anomalies were present with abnormally shaped vertebral bodies and

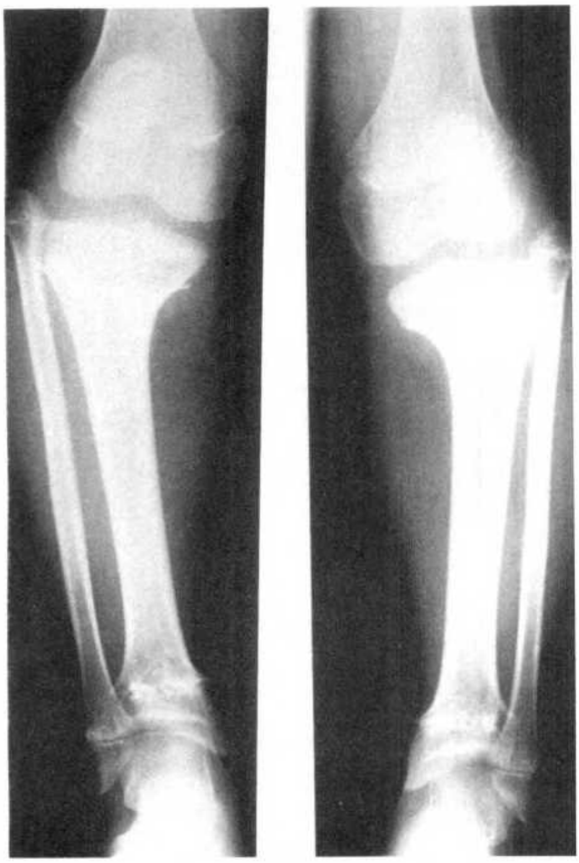

FIG. 4.

Frontal view of both legs at 12 years old. There is remarkable overgrowth of the fibula bilaterally. No cone epiphyses in the fibula are noted. Distally in the ankle region there are metaphyseal changes present in the tibia and fibula. (Bilateral fibular-head excision had been performed 4 years earlier.)

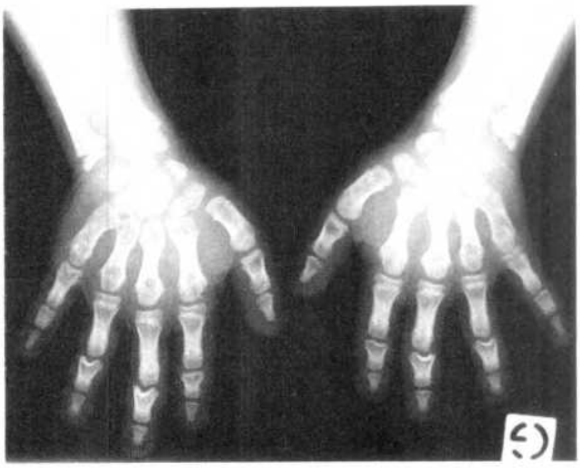

FIG. 5.

Frontal view of both hands at 12 years old. There are fused cone epiphyses of the middle phalanges, bilaterally, of all digits except the thumb. The tufts themselves are somewhat hypoplastic but show no evidence of coning. The metaphyses are abnormal in the proximal phalangeal regions. Cone epiphyses with fusions occurred in the metacarpals as well. The remainder of the bones appear normal.

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hypoplasia of the odontoid process. Accelerated growth was observed during the first year of life; the growth curve decreased during the second year of life with very early subsequent epiphyseal fusion. The patients were unrelated. Bellini et al (1984) reported a case of a new metaphyseal dysplasia of the lower limbs occurring in two male siblings born to healthy, unrelated parents. Clinical and radiological features were short stature, mental retardation, acceleration of bone maturation, cup-shaped widening of the metaphyses, especially around the knees, and cone-shaped widening of the epiphyses. In this case the dyschondroplasia involved mainly the knees and the distal tibiae with cone-shaped epiphyses and cupped metaphyses. The metaphyseal changes were much more prominent, mainly in the femur, than in our case. As in our case, overgrowth of the fibula was observed. The cases of Jequier et al (1981) and Bellini et al (1984) have some radiological features in common with ours, but are not identical. Most of the well known syndromes with metaphyseal defects differ from the condition we describe.

## CONCLUSION

We report what seems to be an unusual case of metaphyseal dyschondroplasia affecting the humerus, hands, tibiae and fibulae and cone-shaped epiphyses of the tibia and phalanges. The bone age is advanced and no other visceral abnormality is present In particular, the patient shows no mental retardation.

ACKNOWLEDGMENT

I wish to thank Doctors Stoker, Giedion, Bellini and Lachman for their help

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# Heterotopic gastric mucosa presenting as small-bowel obstruction

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*(Received May 1986)*

Heterotopic gastric mucosa (HGM) can occur anywhere in the gastrointestinal tract but, other than in Meckel's diverticulum, its occurrence in the small intestine distal to the ligament of Treitz is rare (Lee et al, 1970) Twenty-six such cases have been reported in the literature to date and in most of these the HGM was found in the jejunum Fourteen presented with intussusception, five with haemorrhage, three as perforation, three were asymptomatic and one presented as obstruction in a 3-week-old baby. In this latter case, the obstruction was caused by an associated cyst in the jejunal wall (Sen Gupta & Smith, 1983) We report a case of HGM itself causing intestinal obstruction in a young man.

## CASE REPORT

A previously well, 16-year-old Caucasian boy was admitted with a 6-day history of painless vomiting and constipation following wisdom-teeth extraction under a general anaesthetic On admission he was found to have abdominal distension and hyperactive bowel sounds and was obviously dehydrated (urea 40.4 mmol/l, creatinine 148 μmol/l) Abdominal radiographs confirmed the presence of an upper small-bowel obstruction (Fig 1)

Rehydration, with correction of fluid and electrolyte abnormalities and naso-gastric aspiration were instituted and within 3 days all signs had resolved. Two small-bowel enema examinations were performed, the first showing some dilatation of the proximal jejunum with picket-fencing (Fig 2A) and flocculation of barium (Fig. 2B) The duodeno-

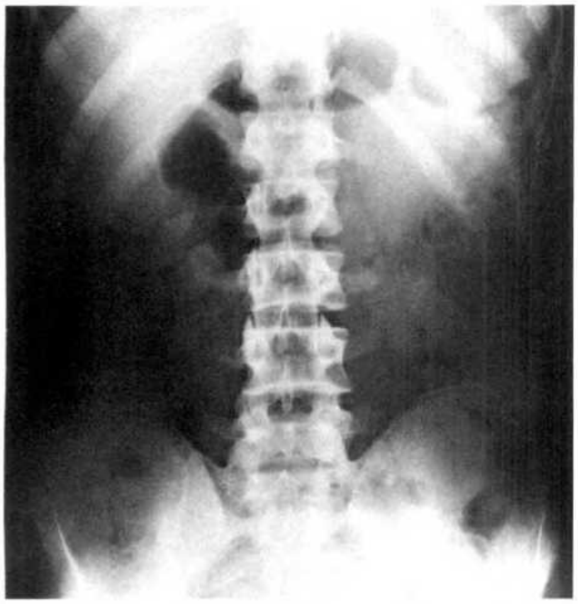


FIG. 1.

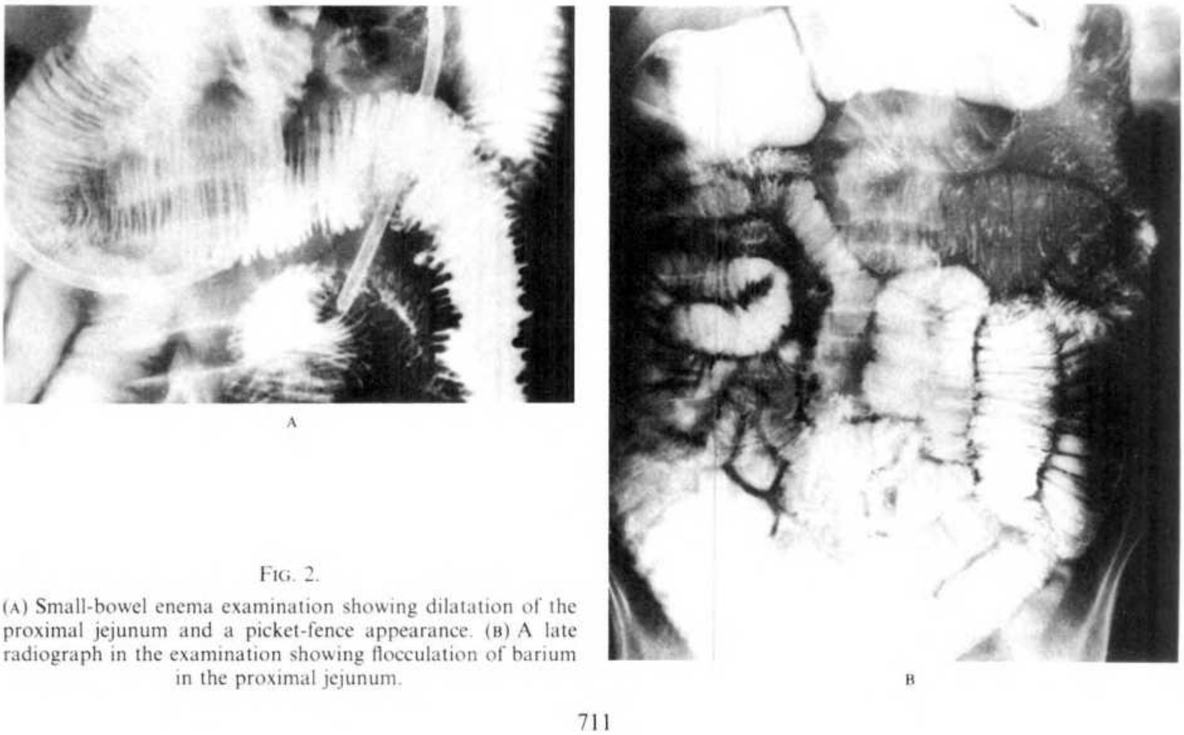
Supine abdominal radiograph showing dilatation of the stomach and duodenum indicating a proximal small-bowel obstruction.

jejunal flexure was not, however, well shown on this study and so a repeat examination was performed 6 days later. This demonstrated a lobulated mass projecting into the lumen of the proximal jejunum from the mesenteric side of the bowel (Fig. 3). At laparotomy, a 9.5 cm polypoid mass, involving half the bowel circumference, was found in the proximal jejunum (Fig. 4). A resection with end-to-end anastomosis was performed and the patient made an uneventful post-operative recovery. Histological examination showed the resected specimen to consist of heterotopic gastric-body type mucosa. The surrounding small-intestinal mucosa was normal.

## DISCUSSION

Heterotopic gastric mucosa is believed to be congenital in origin, arising by differentiation of developmentally displaced pleuripotent cells (Frank, 1983). Other ectopic tissue is acquired and represents metaplastic differentiation during repair and regeneration of injured tissue. There remains much debate over heterotopic and metaplastic aetiologies for all ectopic tissues. Heterotopic tissues may be clinically significant because the ectopic tissue produces symptoms or because it resembles neoplasia in its radiological or endoscopic appearances.

Diagnosis of HGM is often difficult and relies on a combination of radiological, endoscopic and radionuclide techniques. Complications may lead to surgery before these tests can be completed and the diagnosis may not be made until after resection of the lesion. Small-bowel enema is the investigation of choice in the search for small-bowel HGM. This may demonstrate a polypoid filling defect, usually associated with an intussusception if the patient is having pain (McWey et al, 1982). It may be difficult to distinguish such appearances from adenomas, hamartomas or other benign lesions such as angioma, lipoma or carcinoid,


A

B

FIG. 2.

(A) Small-bowel enema examination showing dilatation of the proximal jejunum and a picket-fence appearance. (B) A late radiograph in the examination showing flocculation of barium in the proximal jejunum.

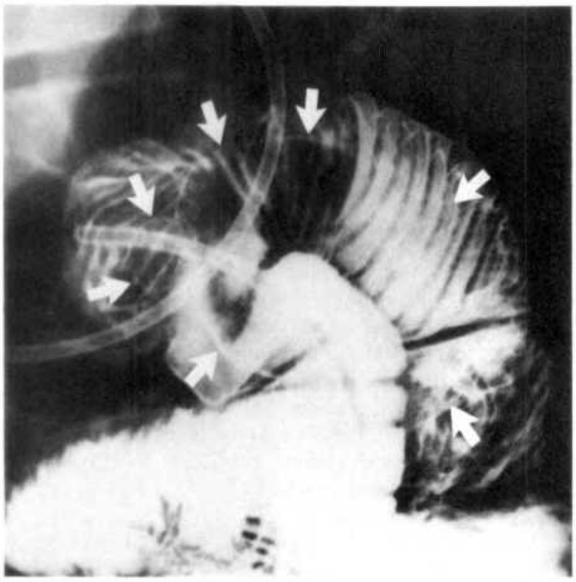


FIG. 3.

The second small-bowel enema examination demonstrated a lobulated mass projecting into the proximal jejunum.

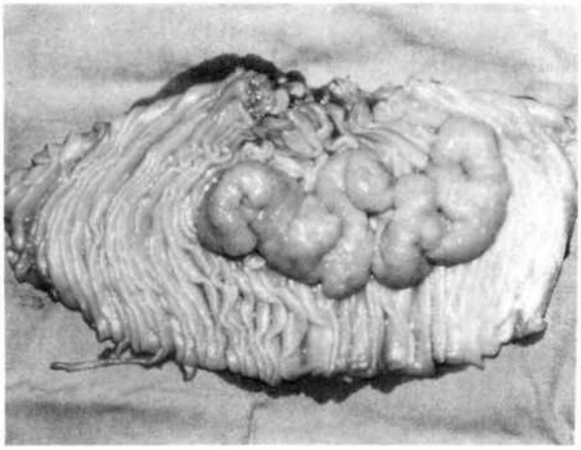


FIG. 4.

Resected specimen showing the mass of heterotopic gastric mucosa.

and malignant tumours such as lymphoma or carcinoma (Reeder & Felson, 1975). The small-bowel enema studies performed on our patient provided clues to the diagnosis. Mucosal oedema and dilatation of the proximal jejunum with flocculation of the barium are changes that are also seen with Zollinger-Ellison syndrome (Marshak & Lindner, 1970) and when seen distal to a mass might suggest the diagnosis of HGM. The possibility was considered that the lesion had intussuscepted with spontaneous reduction as the cause of mucosal oedema, but this was thought unlikely in this patient, as the bowel proximal to the lesion did not appear oedematous and the patient had experienced no pain.

The small-bowel enema had to be repeated as the suspected site of obstruction was not shown on the initial study. Failure to identify the mass on the first study was caused by the end of the tube being passed distal to the duodeno-jejunal flexure.

Abdominal scintigraphy with $^{99}Tc^{m}$ pertechnetate has been used to identify ectopic gastric mucosa in Meckel's diverticulum. This is shown as a well demarcated, persistent focus of high-intensity activity which appears as early as the activity in the stomach. Accumulation of the radionuclide may result from HGM in other parts of the bowel, but to be diagnostic the uptake must appear simultaneously with that in the stomach. One recent series reports such a high degree of accuracy with this investigation (over 90%) that they suggest that a positive scan alone can be used as an indication for laparotomy in patients with suspected bleeding HGM in a Meckel's diverticulum (Stakianakis & Hasse, 1982). It is probable that the same would be true for HGM elsewhere in the gastrointestinal tract.

The final diagnosis of HGM depends on histological findings after endoscopic biopsy or laparotomy. If the lesion is asymptomatic there appears to be no indication for removal. However, HGM of the jejunum and ileum is often symptomatic and its presentation as small-bowel obstruction in association with intussusception is well recognised. This is the first report of HGM presenting with obstruction in the absence of intussusception and serves to illustrate the importance of careful pre-operative assessment in all patients presenting with small-bowel obstruction and demonstrates the use of the small-bowel enema in the investigation of HGM.

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*Case reports*

# Simulated splenic rupture on computed tomography

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*(Received August 1986 and in revised form September 1986)*

Computed tomography (CT) has been shown to be a very accurate method of examining the spleen following trauma (Federle et al, 1981; Jeffrey et al, 1981) and few false positive diagnoses of splenic injury have been reported. A case is presented that was initially misinterpreted as splenic rupture on CT. The reasons for diagnostic confusion in this case are discussed and other causes of false positive diagnosis are reviewed.

## CASE REPORT

A 25-year-old man was seen in the emergency room after being struck by a car. The patient complained of pain in his abdomen, back, left flank and left hip. On physical examination his abdomen was soft, non-tender and bowel sounds were audible. There was a palpable haematoma in the left groin and tenderness on palpation over the pubic symphysis. Urinalysis revealed 3+ haematuria. An intravenous urogram (IVU) demonstrated a normal upper urinary tract, but showed a ruptured bladder with extensive extraperitoneal extravasation. There was no radiographic evidence of intraperitoneal leakage.

The patient continued to complain of diffuse abdominal pain and abdominal CT was performed approximately 1½ h after the IVU. This was performed without intravenous contrast enhancement because the referring physicians were concerned about a high iodine load following the previous urogram. The preliminary interpretation of the CT scan was that there was a ruptured spleen (Fig. 1). Laparotomy demonstrated a normal spleen but 400 ml of urine were drained from the peritoneal cavity.

## DISCUSSION

The main reason for interpretive error in this case was that the normal spleen was not recognised because of its low attenuation value (48–59 HU) relative to the liver (75–81 HU), and was mistaken for a haematoma in the splenic bed (Fig. 1). In addition, the peripheral high-density fluid was compatible with acute haemorrhage, although it was actually intraperitoneal urine containing contrast medium (Fig. 1).

In an attempt to explain the low-density spleen, we postulated that the patient became hypotensive during his IVU and that splenic perfusion was markedly diminished, thus decreasing the amount of contrast medium reaching the spleen. Berland et al (1985) described three patients having low-attenuation spleens following trauma. All had hypotensive episodes before their CT scan. One case resulted in a false positive diagnosis of splenic artery disruption.

The spleen is normally less dense than the liver on a pre-contrast-medium or infusion scan, while on dynamic scans with prolonged injection of contrast medium this relationship is transiently reversed. Berland's cases all showed a splenic enhancement of at least 20 HU less than the hepatic enhancement in the same section. Their cases resembled splenic infarction, but lacked several findings seen commonly with infarction, namely a preserved rim of enhanced tissue, splenic enlargement, focal, wedge-shaped defects and vascular thrombosis. They postulated the cause of decreased splenic enhancement as diminished perfusion from sympathetic stimulation following trauma. Concurrent hypotension may have also been necessary to diminish splenic perfusion. Hepatic blood flow, on the other hand, is probably not significantly altered following trauma because of the liver's dual blood supply and because of the lesser effect of sympathetic stimulation on the liver.

Our case is not actually comparable with Berland's cases because our scan was performed without intravenous contrast enhancement. We had, in effect, performed a delayed iodine scan, because an IVU had been performed 1½ h before the CT scan. Chamberlain and Sherwood (1966) and Becker et al (1968) have shown that the liver normally excretes 1–2% of an

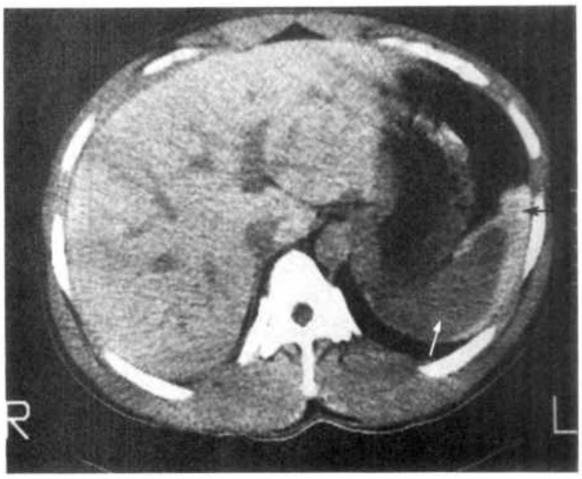

FIG. 1.

An axial scan of the upper abdomen demonstrates an apparent low-density haematoma in the splenic bed (white arrow), surrounded by high-density fluid (black arrow) compatible with fresh haemorrhage.

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injected iodine dose through the biliary system We were unfamiliar with the appearance of a delayed iodine scan and saw the spleen as being abnormally low in density, while it was the liver that was appropriately high in density. Bernardino et al (1986) and Phillips et al (1985) have shown that delayed iodine scanning of the liver increases conspicuity of hepatic metastases by increasing the density of normal liver, while metastases decrease to pre-contrast levels. Phillips et al (1985) showed that the liver attenuation increased by an average of 22 HU 4 h after administration of 58.4 g of iodine (200 ml of 60% meglumine diatrizoate).

Jeffrey et al (1981) reviewed CT scans of 50 patients following abdominal trauma and correctly diagnosed 21 of 22 splenic injuries. They had one false positive case, a 4-year-old girl who had a small spleen, paucity of perisplenic fat and rib artefacts They described other potential pitfalls including motion and streak artefacts and splenic clefts Clefts can be distinguished from lacerations because they are along the medial aspect of the spleen and have a thin, linear configuration. Subcapsular haematomas and lacerations almost always involve the lateral aspect of the spleen and have associated free intraperitoneal blood. Jeffrey et al (1981) also encountered a perisplenic abscess that simulated a subcapsular haematoma. The medial location of the collection and secondary signs of inflammation helped in making the correct diagnosis

A final pitfall was described by Cholankeril et al (1984), who had three cases in which the left lobe of the liver simulated a perisplenic haematoma. This pitfall can be avoided by carefully tracing the perisplenic density to its connection with the left lobe of the liver. In addition, other signs of splenic laceration will not be present.

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# Negative gallium scan in an AIDS patient with *Pneumocystis* pneumonia

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(*Received April 1986 and in revised form October 1986*)

Patients with acquired immune deficiency syndrome (AIDS) and *Pneumocystis* pneumonia may present with subacute illness, a normal chest radiograph, and normal arterial blood gases (National Heart, Lung and Blood Institute, 1984, Kovaks et al, 1984; Hattner et al, 1985). The decision to utilise invasive diagnostic techniques, such as fibreoptic bronchoscopy or open lung biopsy during thoracotomy, with their attendant risks, is difficult in patients without obvious pulmonary dysfunction. Some investigators have reported that scans with gallium-67 citrate (gallium scan) were abnormal in the pulmonary area of all AIDS patients with *Pneumocystis* pneumonia before specific treatment (Barron et al, 1985; Coleman et al, 1985; Hattner et al, 1985). Such an extremely sensitive screening test, with at least moderate specificity in AIDS patients, would be very useful for investigation of these patients. We report on an AIDS patient with documented *Pneumocystis* pneumonia who had a gallium scan interpreted as negative before initiation of specific treatment, illustrating that the gallium scan is not completely sensitive for detection of *Pneumocystis* pneumonia. However,

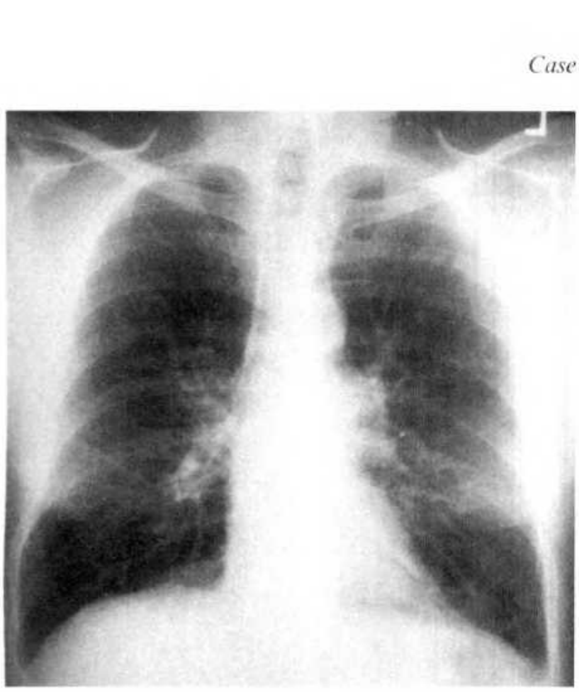

FIG. 1.

Chest radiograph of January 1985 reveals opacities in lingula and left lower lobe. A chest radiograph 3 weeks earlier was unremarkable.

pulmonary gallium uptake during pneumonia was greater than in a baseline gallium scan, indicating the value of serial scans.

### CASE REPORT

A 58-year-old black male abuser of intravenous heroin presented to the Martinez VAMC in December 1983 with cough, dyspnoea on exertion, and progressive bilateral parenchymal opacities on chest radiograph. *Pneumocystis* pneumonia was diagnosed by demonstration of the organism on a touch preparation of a transbronchial biopsy obtained during fibreoptic bronchoscopy. After prompt clinical and radiographic response to 28 days of intravenous trimethoprim–sulfamethoxazole (TMP/SMX), he was instructed to take TMP/SMX orally indefinitely as "prophylaxis." At this time, T-cell studies showed a helper-to-suppressor cell ratio of 0.14.

In January 1985 the patient became short of breath and developed a dry cough. Chest radiograph showed lingular and bilateral lower-lobe opacities. After his symptoms failed to respond to oral ampicillin, he was admitted to Martinez VAMC. He had stopped taking TMP/SMX in the autumn of 1984 because of a rash.

Lingular and left lower-lobe parenchymal densities (Fig. 1) had progressed when compared with the radiograph obtained 3 weeks previously. Arterial blood gases obtained while breathing room air were PaO$_2$ 39 mm Hg, PaCO$_2$ 29 mm Hg, and pH 7.49. Other laboratory data were unremarkable.

Methenamine silver stain of a touch preparation of a transbronchial biopsy obtained on the second day in hospital demonstrated moderate to large numbers of *Pneumocystis* organisms. On the third day in hospital, TMP/SMX was administered intravenously to the patient, whose symptoms improved markedly, and he was discharged on the 21st day with instructions to continue TMP/SMX orally. Chest radiograph at the time of discharge showed marked resolution of parenchymal densities and arterial blood gas obtained at time of discharge were PaO$_2$ 82 mm Hg, PaCO$_2$ 31 mm Hg, and pH 7.55 while breathing room air.

On the first day in hospital of the second admission, 229 MBq (6.2 mCi) of gallium-67 citrate was injected intravenously. He was scanned 48 h later with anterior and posterior total body scans and detailed views of the abdomen, with anterior view shown in Fig. 2. Uptake in the lung was less intense than uptake in the liver but greater than that in soft tissues. This scan was interpreted as negative but, in retrospect, lung uptake of gallium, relative to liver, on a scan in October 1984, when the patient was asymptomatic, was even less (Fig. 2A).

### DISCUSSION

Gallium scans have been strikingly successful in the detection of *Pneumocystis* pneumonia in AIDS patients. In a study of 21 patients with AIDS and pulmonary symptoms, all 11 patients with *Pneumocystis* pneumonia had abnormal gallium scans (lung uptake greater than or equal to liver uptake) as assessed by blind interpretation (Hattner et al, 1984a, 1985; Coleman et al, 1985). The same investigators performed a second study of 14 AIDS patients with *Pneumocystis* pneumonia that included four patients with normal chest radiographs and/or normal PaO$_2$, and found that gallium scans were abnormal in all 14 patients (Hattner et al, 1984b). In a recent study of eight patients with *Pneumocystis* pneumonia, all had markedly positive scans when obtained prior to therapy (Tuazon et al, 1985). In another report of 18 AIDS patients with *Pneumocystis* pneumonia, including six with normal chest radiographs, 17 had abnormal gallium scans (Barron et al, 1985). The single patient with a normal gallium scan in the presence of *Pneumocystis* pneumonia had received specific treatment that had started 14 days before the scan. Specific treatment is known to cause reversion of gallium scans to normal (Hattner et al, 1984b; Coleman et al, 1985). Thus, gallium scans were considered virtually 100% sensitive for detection of *Pneumocystis* pneumonia and of particular value in the investigation of patients with normal or equivocal chest radiographs, normal arterial blood gases, or minimal symptoms.

In the context of AIDS, a gallium scan that demonstrates abnormal activity in the pulmonary area is moderately specific for *Pneumocystis* pneumonia. Specificities of 90% (Hattner et al, 1984a, 1985; Coleman et al, 1985) and 74% (Barron et al, 1985) have been calculated for abnormal gallium scans.

Negative gallium scans in patients with *Pneumocystis* pneumonia are apparently rare. A Grade 2 gallium scan (pulmonary uptake less than liver uptake but greater than that of soft tissue) was reported for an AIDS patient with a normal chest radiograph, normal PaO$_2$, "minimal symptoms" and *Pneumocystis* organisms demonstrated in a bronchoscopy specimen (Hattner et al, 1985). It is unclear from the report whether the patient had pneumonitis, and *Pneumocystis* organisms

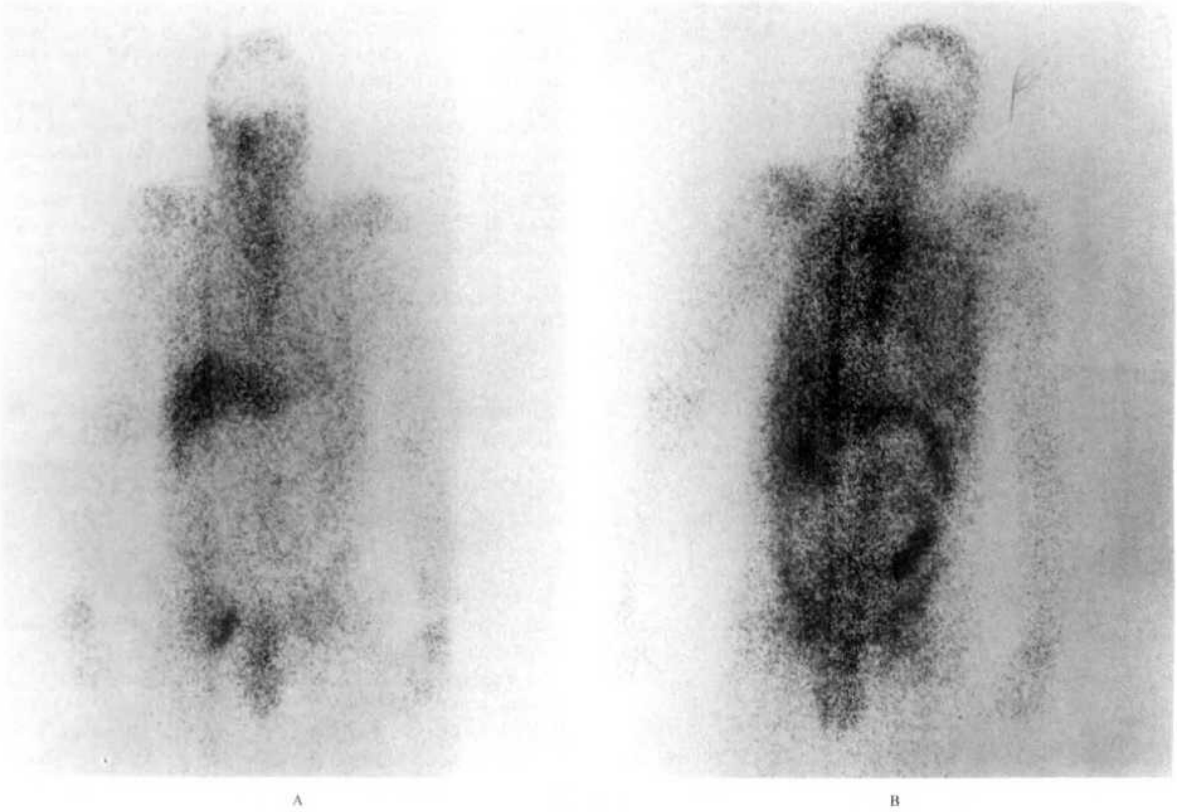

FIG. 2.

(A) "Baseline" gallium scan (anterior view) of September 1984 when patient was asymptomatic. Area of uptake in right groin reflects inflammation at intravenous injection site. (B) Gallium scan (anterior view) of February 1985, when patient had *Pneumocystis* pneumonia.

may persist in the lung despite appropriate, successful, specific treatment (Shelhamer et al, 1984), particularly in AIDS patients (National Heart, Lung and Blood Institute, 1984). The sensitivity of gallium scans for detection of *Pneumocystis* pneumonia was 98% from the data at this workshop.

The patient in this report had florid *Pneumocystis* pneumonia, as assessed by symptoms, progressively abnormal chest radiographs, profound hypoxia, demonstration of large numbers of *Pneumocystis* organisms on a transbronchial biopsy specimen, and clinical response to therapy with TMP/SMX. The decision to pursue invasive studies in our patient was relatively easy, given the obvious extent of pulmonary disease and previous history of AIDS and *Pneumocystis* pneumonia.

The reasons for the gallium scan being only Grade 2 are not apparent. Gallium scans falsely negative for purulent infectious processes have been reported previously, and often no cause for the negative scans was obvious (Hopkins et al, 1975, Caffee et al, 1977; Handmaker & O'Mara, 1977). Localisation depends upon delivery of gallium to the site, which may be a function of: leucocyte labelling; blood supply; protein binding, particularly to transferrin (Hoffer et al, 1977); degree of inflammation (Line et al, 1985) and uptake by the pathogen (Tsan et al, 1977). In our patient, we have no reason to suspect a technical problem with the gallium label, and the patient did not have leucopenia. Transferrin levels were not determined, but other haematological findings did not indicate iron deficiency, and he had no gross abnormalities in levels of serum proteins. Organisms such as *Staphylococcus aureus* have been reported to take up gallium (Tsan et al, 1977), but we are unaware of similar studies for *Pneumocystis carinii*. Since gallium scans are usually positive in AIDS patients with *Pneumocystis* pneumonia, lack of uptake by the organism would not usually be critical. Mechanisms of gallium localisation in inflammatory lesions and possible reasons for lack of localisation have been discussed in a recent article (Tsan, 1985).

Although gallium scans are useful for screening AIDS patients for pulmonary diseases, a Grade 2 gallium scan, by current interpretive criteria, does not eliminate

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the possibility of *Pneumocystis* pneumonia. A baseline scan may prove helpful in detecting subtle differences in lung uptake over time. Computer analysis using regions of interest over the liver, lung, and soft tissue, as has been done in sarcoid, may help in the quantification of these subtle changes over time which do not result in definitely abnormal studies using standard interpretive criteria (Gupta et al, 1982; Line et al, 1985)

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# Misleading technetium-99m DTPA renogram in renal carcinoma

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(*Received May 1986 and in revised form August 1986*)

In most renal disorders there is good agreement between estimates of relative renal function made using $^{99}$Tc$^{m}$ DTPA and $^{99}$Tc$^{m}$ DMSA scintigraphy (Bingham & Maisey, 1978; Taylor, 1982). In this report we describe the case of a patient with a known right renal carcinoma (hypernephroma) in whom an estimate of relative renal function was required before surgery. Compared with quantitative static $^{99}$Tc$^{m}$ DMSA scintigraphy, $^{99}$Tc$^{m}$ DTPA gamma-camera renography was shown to overestimate significantly the functional contribution of the affected kidney. The reason for the

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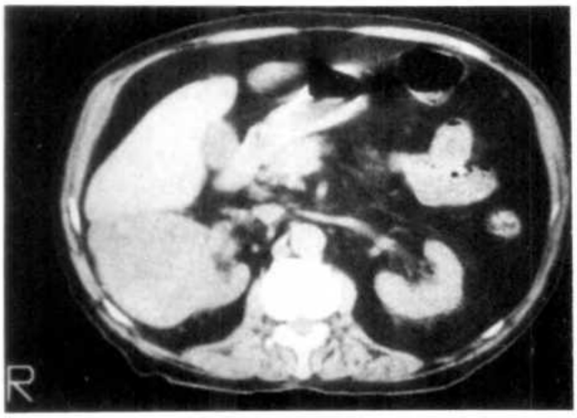

FIG. 1.

Computed tomography scan at the level of the right renal tumour (L = +51, W = 500).

discrepancy was attributed to the high vascularity of the tumour and surrounding tissues.

### CASE REPORT

A $^{99}$Tc$^{m}$ DTPA renogram was requested as a pre-surgical test for a 76-year-old man with a right renal carcinoma. The tumour had been recently diagnosed on intravenous urography and subsequently definitively demonstrated by computed tomography (CT) (Fig. 1). The serum urea level before surgery was 16 mmol/l (normal range 2.5–6.5 mmol/l). A standard gamma-camera renogram was performed (patient supine) using 250 MBq of $^{99}$Tc$^{m}$-calcium trisodium-DTPA chelate. Regions of interest were subsequently defined using a summed image (1–3 min post-injection) and background-subtracted whole-kidney renograms generated (Fig. 2). Comparing the amplitudes of the renograms during the second phase produced a value of 76% for the functional contribution of the affected kidney.

The rather unusual distribution of activity within the right kidney, together with the surprisingly high value for its functional contribution, led us to perform a static $^{99}$Tc$^{m}$ DMSA renal scan as an alternative means of estimating the relative function of the affected kidney. The DMSA scan was performed 24 h after the DTPA study. A single dose of 78 MBq of $^{99}$Tc$^{m}$ DMSA was withdrawn from a vial of the agent prepared 15 min earlier. Injection was made almost immediately and static imaging of the kidneys was commenced after 2 h. It was apparent that the intrarenal distributions of DTPA and DMSA within the right kidney were quite different. Unlike the DTPA images, there was little uptake of DMSA in the region of the right kidney occupied by the tumour (Fig. 3). For direct comparability with the DTPA images, and also because of interference from overlying liver activity on the anterior view (not shown), the estimate of relative DMSA uptake was made using the posterior view alone. Regions of interest were defined for the left kidney, right kidney (excluding tumour) and a background area (between the kidneys). After appropriate background subtraction, relative DMSA uptake for the right kidney was found to be 42%. In the light of the DMSA study, the region of interest on the DTPA scan for the right kidney was redrawn to exclude the area occupied by the tumour. This procedure, although obviously reducing the overestimation of right kidney function

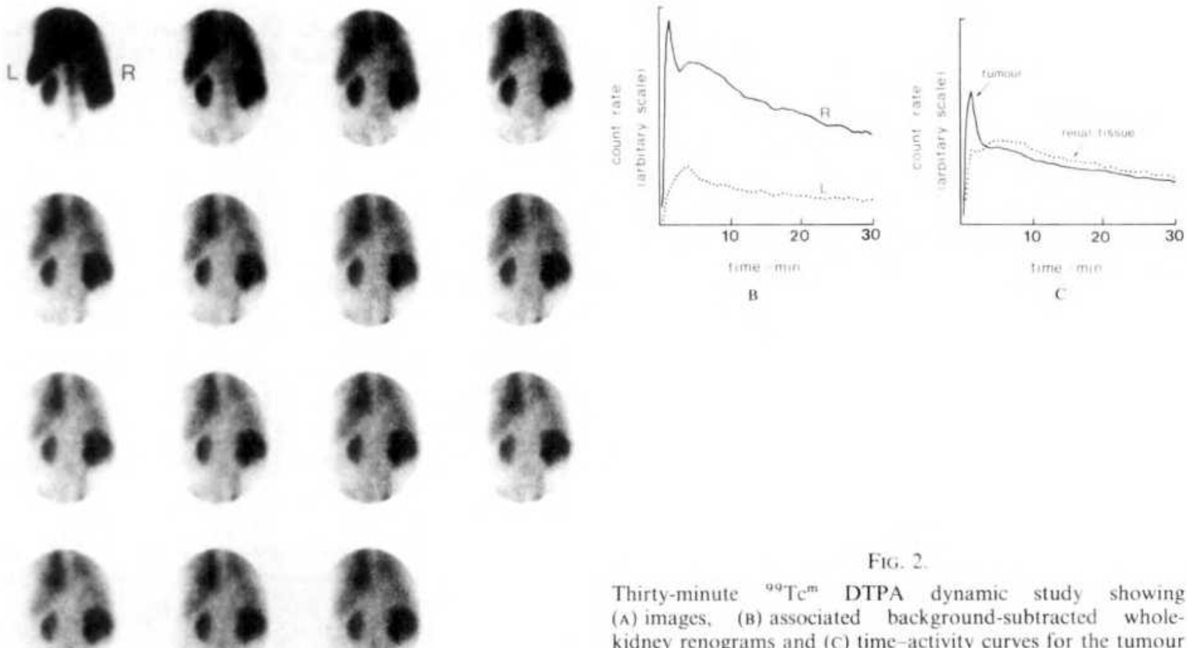

FIG. 2.

Thirty-minute $^{99}$Tc$^{m}$ DTPA dynamic study showing (A) images, (B) associated background-subtracted whole-kidney renograms and (C) time–activity curves for the tumour and adjacent renal tissue. The "right kidney" curve shown in (B) is a composite of these two curves, one purely vascular and one functional.

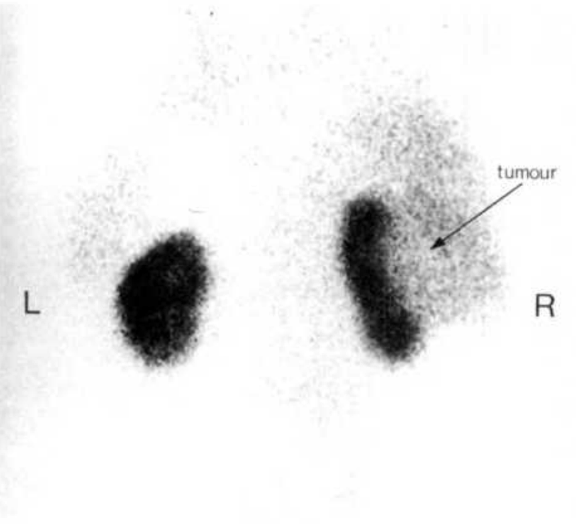

FIG. 3.

Technetium-99m DMSA posterior image acquired 2 h after injection. Uptake in the right renal tumour is only slightly greater than that in the liver.

(from 76% to 58%) still did not produce a value consistent with the DMSA scan estimate (42%). It was evident from the two "right kidney" curves (including and excluding the tumour) that the whole-kidney renogram originally used for the estimation of relative renal function (Fig. 2B) was a composite of a purely vascular curve, derived from the tumour, and a recognisable renogram from the adjacent renal tissue (Fig. 2C).

A total right nephrectomy was duly performed and histological examination of the mass showed it to be a classic clear-cell Grawitz tumour (hypernephroma). The patient made an uneventful post-operative recovery and was allowed home after a short convalescence. His serum urea level on discharge was 12 mmol/l.

## DISCUSSION

No radiopharmaceutical specific to renal tumours is yet known. Renal tumours, like other space-occupying lesions, usually appear as areas of reduced or absent activity on gamma-camera images using kidney radiopharmaceuticals (O'Reilly et al, 1979).

We have described the case of a 76-year-old man with a right hypernephroma in whom a $^{99}$Tc$^{m}$ DTPA study showed persistently increased activity in the vicinity of the tumour, whereas a $^{99}$Tc$^{m}$ DMSA scan showed essentially absent uptake. The former observation was eventually reconciled with a simple, although unusual, manifestation of a purely vascular phenomenon but, without the benefit of the intravenous urogram on CT scan, was originally misinterpreted as genuine uptake resulting in the tumour being included in the right kidney region of interest. The functional contribution (to total glomerular filtration rate) of the affected kidney was therefore grossly overestimated.

It is known that hypernephromas are frequently associated with a marked increase in vascularity, both in the tumour itself and in the surrounding tissue. The latter may explain why, even after "excluding" the tumour from the right kidney region of interest, the DTPA study still overestimated its relative function.

It is acknowledged that, in this case, the outcome of the radionuclide studies had no immediate effect on patient management; providing the contralateral kidney is functioning, a total nephrectomy would nearly always be performed for renal carcinoma. The renogram did, however, provide proof that the function of the contralateral kidney was indeed normal. Radionuclide studies may, however, be requested in more demanding circumstances and it is important to be aware of the potential pitfalls associated with the alternative methods of estimating relative kidney function in renal carcinoma.

Finally, as an added complication, it should also be remembered that genuine uptake of both DTPA and DMSA may occasionally occur in renal carcinomas (Pion et al, 1976; O'Reilly et al, 1979). Such rare instances would, for the purposes of estimating relative renal function, pose an even greater problem than the one referred to in this report.

In conclusion, if DTPA is used in this context, it is imperative that the intravenous urogram and CT scan are consulted before analysing the radionuclide study for accurate exclusion of the tumour from the region of interest. On balance, it is recommended that static $^{99}$Tc$^{m}$ DMSA scintigraphy is used in preference to $^{99}$Tc$^{m}$ DTPA renography in attempting to estimate relative kidney function in known renal carcinoma.

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# Book reviews

*NCI Monographs 1986 No. 2. Cancer Control Objectives for the Nation 1985–2000* Ed by Peter Greenwald and Edward J. Sondik, pp. xv + 105, 1986 (National Cancer Institute, Bethesda, USA), $7.50.
Stock No 017-042-00191-9

This monograph is based on the deliberations of four working groups which considered prevention, screening, treatment and surveillance of cancer The first three working groups were to set objectives for their respective areas of concern, while the surveillance group was to identify measures of progress and evaluation strategies. The monograph sets out some general points in relation to cancer control objectives and the key points stemming from the deliberations of the four working groups.

Under "Prevention", brief comments are made about the role of lifestyle factors, environmental factors, and genetic factors. Emphasis is placed on the controllable risk factors· tobacco, diet, and occupational exposure. The potential impact of prevention in relation to these three aspects is discussed, and then quantified in terms of lives that could be saved

As far as screening is concerned, the only two conditions where it was thought to be demonstratively effective were breast cancer and cervical cancer, and for the former only in women over the age of 50 years. The impact is thought to be uncertain for prostate, oral, testicular, colorectal, bladder, endometrial, oesophogeal, and gastric cancer and for melanoma and breast cancer in women aged 40–49 years. The impact of breast self-examination, at any age, is also uncertain

The US national system for collecting 5-year survival rates was discussed and the trends in these statistics for patients treated in 1960 through to 1981 were presented It was emphasised that there were discrepancies between the national survival data and results from large Phase-III clinical trials It was suggested that the national data represented average current treatment, while data from clinical trials describe the achievable state-of-the-art therapy. It was accepted that data from clinical trials may relate to a biased (younger and healthier) subgroup of patients, but did present goals for treatment objectives Also, it was argued that there was no evidence to suggest that widespread dissemination of state-of-art treatment results had been achieved, or that the most effective therapies had reached a desirable maximum level A table set out the treatment objectives for 1990 and 2000, including the types of treatment recommended by site and the improvement in 5-year survival anticipated This was then converted to an estimate of the number of lives that might be saved by the year 2000.

The section on surveillance set out the types of statistics that were warranted in order to monitor cancer control programmes These ranged from mortality, incidence, and survival statistics to data on prevention, screening and treatment.

Bringing together the above results, it was suggested that by the year 2000 a reduction in the cancer mortality rate by as much as 50% was possible if the recommendations regarding smoking reduction, diet change, screening, and dissemination of state-of-the-art treatment were all effectively applied, and there was a continued advance in cancer patient survival through improvement in treatment.

The monograph thus presents points of interest for all those concerned with cancer control. It is clearly presented, relatively short, and reasonably priced. It is just the type of work to borrow from a library and read fairly quickly, as a background to considering present performance in countries other than the US and planning new initiatives M. R. ALDERSON

*Female Breast Examination A Theoretical and Practical Guide to Breast Diagnosis.* By Claude Annonier, pp. xiii + 228, 1986 (Springer-Verlag, Berlin), DM98.
ISBN 3-540-16302-6 (Berlin)
0-387-16302-6 (New York)

It requires an effort to read this book, the study is staccato with a format of notes, lists, tables and many diagrams. Myriad small symbols punctuate the text as an aid to rapid reference The book is concerned essentially with the diagnosis of breast disease in the clinical situation and aims to describe a comprehensive diagnostic strategy using many different techniques The technical descriptions are necessarily superficial and include diaphanoscopy, diaphanometry, ultrasonography, galactography, cystography, mammography, thermography and telethermography The second half of the book provides a comprehensive list of breast diseases and then lists and describes the findings in the different modalities that can be used for diagnosis

The philosophy that if enough investigations are performed, the correct diagnosis will emerge is dubious; not least because some of the investigations may be unreliable. Thermography, for example, has been tried and found wanting but it still has its devotees who cling to it as an act of faith. Cystography and galactography are now rarely used and diaphanoscopy lacks sensitivity and specificity in diagnosis. This book unwittingly illustrates the problems that are generated by embracing new technology before it has been fully and carefully evaluated and shares the reluctance of many to discard outdated techniques Occam's razor, "It is vain to do with more what can be done with fewer" needs to be remembered by those reading this book.

J L PRICE

*Cerebral Ischaemia. A Neuroradiological Study.* Ed by J Bories, pp. 150, 1985 (Springer-Verlag, Berlin), DM128
ISBN 3-540-16158-9 (Berlin)
0-387-16158-9 (New York)

This monograph has already been published as No 6 of Volume 27 of the journal *Neuroradiology* and will, therefore, already be familiar to most neuroradiologists It is a well balanced presentation of the subject by experts involved in the day-to-day diagnosis and practical imaging of cerebral ischaemia. Most of the contributions are from France and reflect the high standard of technical expertise and clinical application which we have come to associate with French neuroradiology The clinical considerations, pathology and pathophysiology are briefly, but very adequately, covered Most space is given to detailed discussion of the currently most applicable techniques (computed tomography and conventional and digital subtraction angiography) but ultrasonography and positron emission tomography are covered and there is a basic consideration to the contribution of magnetic resonance imaging by Michael Brant-Zawadzki and the San Francisco group There are excellent articles on cardiogenic strokes, ischaemic strokes in children, venous infarction and angiographic control and appearances following surgery

The book is lavishly illustrated with radiographs and diagrams, all of which are of excellent quality Interesting new material is used as the basis of a good review which deserves to be widely read by radiologists and clinicians dealing with stroke patients as well as by neuroscientists in training.

B. E KENDALL

1987, *The British Journal of Radiology*, 60, 721–722 JULY 1987

# Case of the month

## The case of the bloated nurse

By J. E. Jackson, M.R.C.P. and A. M. K. Thomas, B.Sc., M.R.C.P., F.R.C.R.

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(*Received August 1986*)

A 46-year-old staff nurse who had been treated at this hospital for several years presented with a history of a severely bloated feeling after meals, with resultant loss of appetite and weight. She had previously suffered from dysphagia secondary to a benign oesophageal stricture which had improved after oesophageal dilatation several months previously. Her abdominal radiograph on admission is shown in Fig. 1. She subsequently had a barium meal and follow-through examination (Fig. 2).

What features are seen and what is the likely diagnosis?

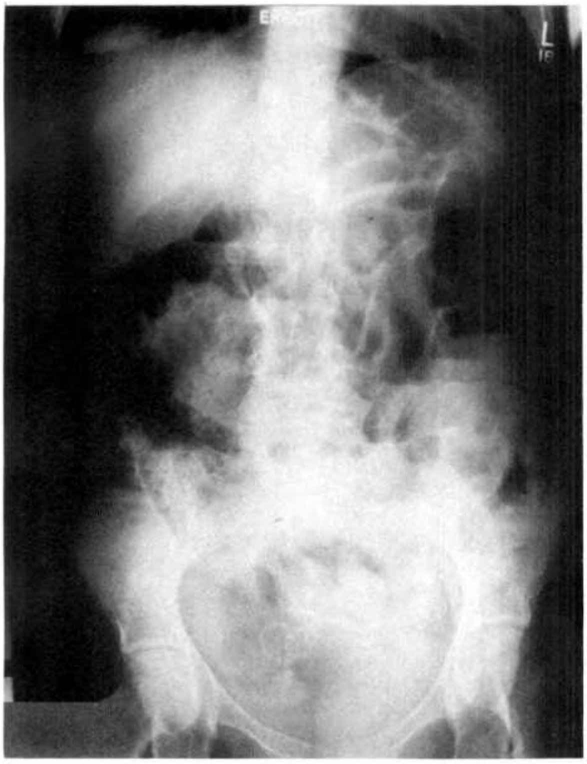
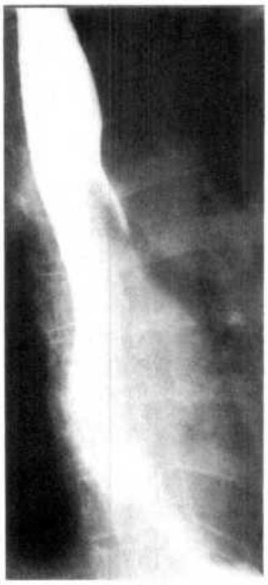


FIG. 1.

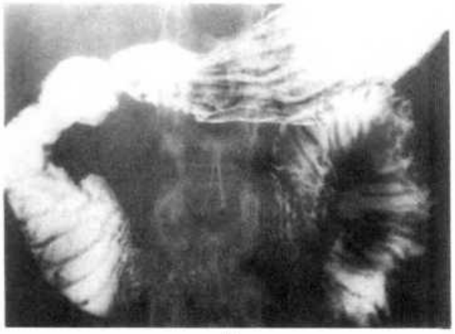
Erect abdominal radiograph.



A

FIG. 2.

Series of radiographs from barium meal and follow-through: (A) oesophagogram, (B) duodenal loop, (C) small bowel, and (D) detail from small-bowel study.



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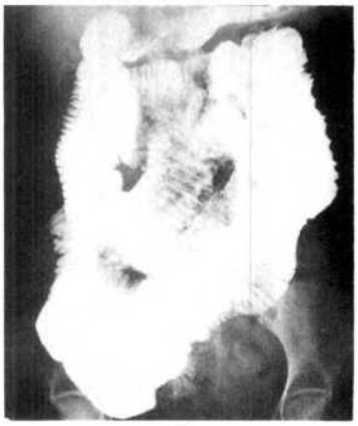

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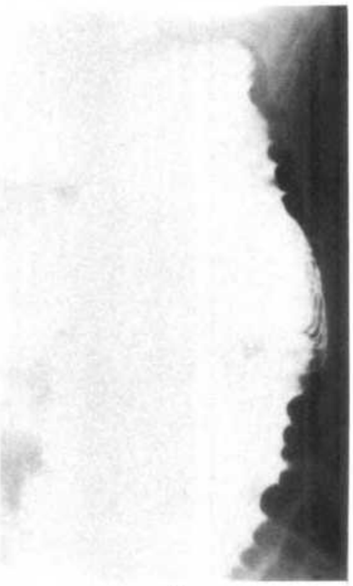

D

The plain abdominal radiograph (Fig. 1) shows small-bowel dilatation and intramural pneumatosis. A barium study shows oesophageal, duodenal and jejunal dilatation with gastro-oesophageal reflux and a diminished transit time. Intramural air is seen clearly in the barium-filled small bowel.

The patient has severe systemic sclerosis and has been treated for Raynaud's phenomenon. She has atrophy of the soft tissues of the fingers with acro-osteolysis (Fig. 3) and basal pulmonary interstitial fibrosis (Fig. 4).

## DISCUSSION

This patient shows the classic features of scleroderma (progressive systemic sclerosis). The oesophagus is usually involved, the small intestine less commonly. Pseudodiverticula may be seen in the large bowel. Small-bowel involvement in scleroderma is associated with a worse prognosis. Meihoff et al (1968), while recognising that intestinal pneumatosis was probably a benign complication, saw it as a grave prognostic sign. The intramural gas is probably produced by the raised intraluminal pressure secondary to diminished intestinal motility forcing gas into the submucosa and subserosa; occasionally there may be an associated pneumoperitoneum (Meyers et al, 1977). It is interesting to note that oesophageal stenosis secondary to caustic (lye) ingestion is a cause of pneumatosis (Koss, 1952) although at the time of presentation the oesophageal stricture was no longer a problem with our patient. Gas in the bowel wall has usually been attributed to primary and secondary causes. In the primary form, called pneumatosis cystoides intestinalis, gas-filled non-communicating cysts are seen in the colon of adults. In a secondary form, linear streaks of gas are seen in the walls of the large or small bowel. In a patient with acute symptoms, the presence of linear gas is usually ominous because it implies the presence of bowel infarction. However, more benign causes of intestinal linear pneumatosis are increasingly being recognised (Table I). A knowledge of the causes of linear pneumatosis may save the patient an unnecessary laparotomy if the clinical features are appropriate. It may be difficult to exclude vascular ischaemia by clinical features and a plain radiograph alone, and in these cases angiography or a water-soluble contrast-medium study may be indicated.

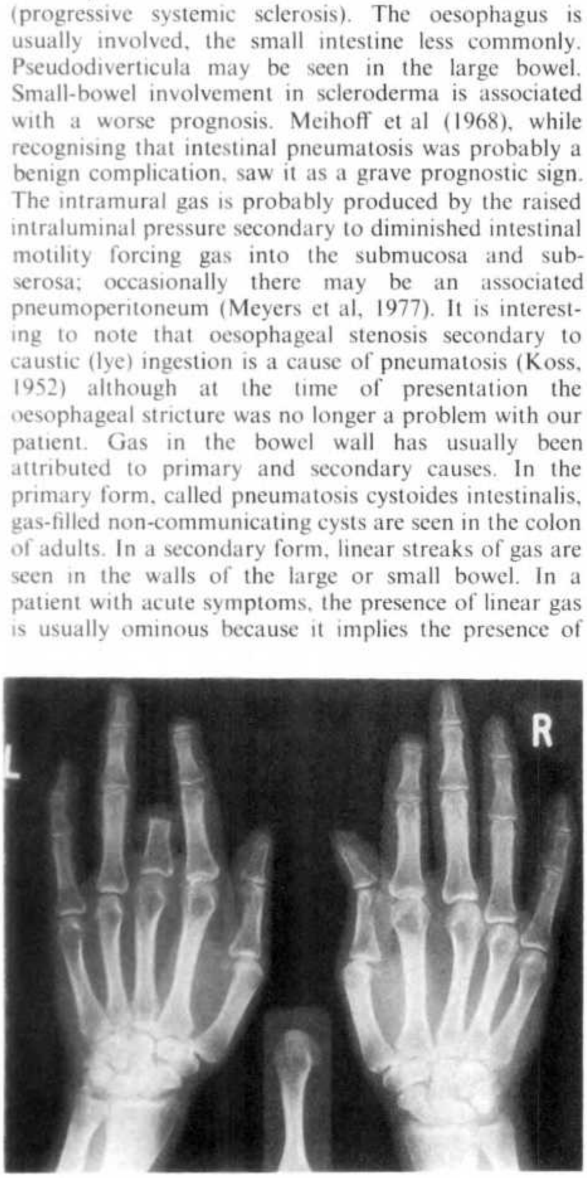

FIG. 3.

Hands of patient showing acro-osteolysis (the left middle finger had to be surgically removed).

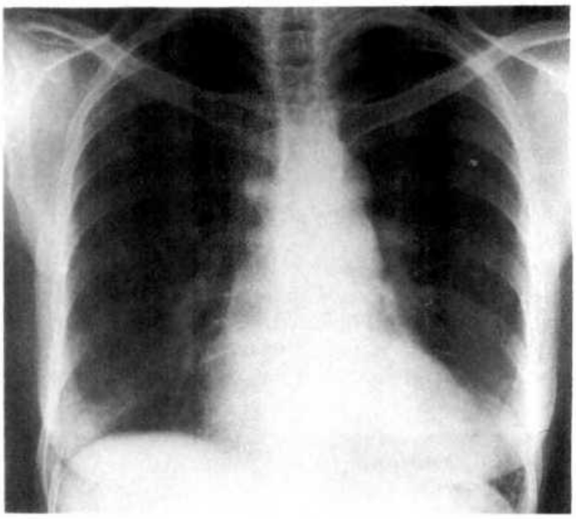

FIG. 4.

Chest radiograph showing basal interstitial shadowing.

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### TABLE I

CAUSES OF LINEAR PNEUMATOSIS

Bowel infarction
Small-bowel obstruction
Collagen vascular disease
Peptic ulceration
Post-endoscopy
Post-bowel anastomosis
Steroid therapy
Necrotising enterocolitis
Carcinoma
Gastric-outlet obstruction
Whipple's disease
Perforated jejunal diverticula
Caustic ingestion
Phlegmonous gastritis
Intestinal parasites
Toxic megacolon

Information from Bryk (1973), Rice et al (1982) and Meyers et al (1977).

1987, *The British Journal of Radiology*, 60, 723–724 JULY 1987

# Short communication

## Compartmentalised depletion of glutathione in cells treated with buthionine sulphoximine

By Margareta Edgren and L. Révész

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(*Received December 1986*)

Evidence obtained in different types of experiments has indicated that glutathione (GSH) can function as an inherent protector of cells against treatment with radiation and many chemotherapeutic agents (Arrick & Nathan, 1984). In an attempt to enhance the effect of such treatments, efforts have been made to control the cellular GSH content artificially. In many of the recent studies, buthionine sulphoximine (BSO) has been used to deplete cellular GSH (Chemical Modifiers of Cancer Treatment, 1986). This substance inhibits the synthesis of gamma-glutamyl-cysteine, a precursor of GSH, by specifically blocking the synthesising enzyme. Edgren (1987) reported observations which suggest that depletion of GSH by BSO occurs to different extents in the nucleus and the cytoplasm. The experiments reported here confirm the earlier observations either when treatment is made with BSO at a single concentration for varying time periods, or at varying concentrations for a fixed period.

Non-confluent cultures of Chinese hamster V79–379A cells were propagated under standard tissue-culture conditions in Eagle's medium with Earle's salts, supplemented with 15% fetal calf serum and antibiotics. Nuclei were isolated according to the method of Nusse and Kramer (1984) involving hypotonic treatment with a detergent, modified slightly as described earlier (Edgren, 1987). Glutathione was measured by the DTNB-glutathione reductase method according to Griffith (1980), except that the acidic extraction was made with 5% TCA.

The concentration of GSH in the BSO-untreated whole cells and their nuclei was $53.0 \pm 7.3$ nmol/$10^7$ cells and $0.24 \pm 0.04$ nmol/$10^7$ nuclei, respectively (mean ± standard error). The relative decrease of GSH after a 3 h treatment with BSO at concentrations of 0.01–10.0 mM is illustrated in Fig. 1. It shows that GSH is depleted from whole cells more efficiently than from isolated nuclei. A concentration between 0.01 mM and 0.1 mM is sufficient for a 50% depletion in the whole cells, but about 10 mM is needed for the same effect in the nuclei during a similar treatment period. When treatment is made with 0.1 mM BSO for varying periods, a delayed depletion of GSH can be noted from the isolated nuclei, reaching the 50%

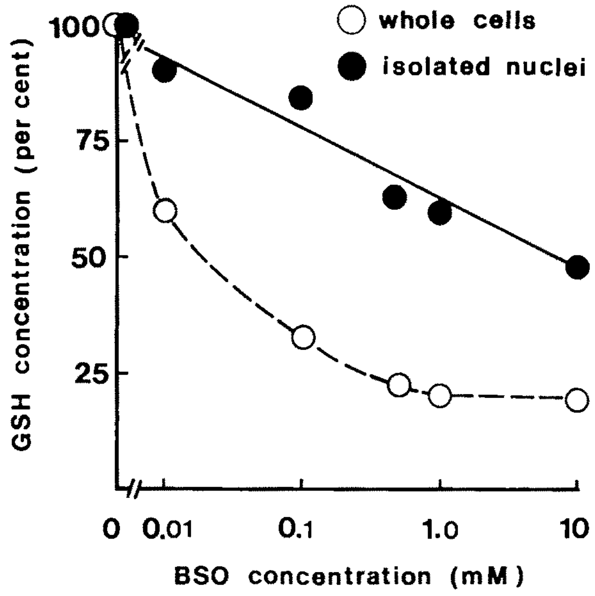

FIG. 1.

The level of GSH in whole cells and corresponding isolated nuclei after 3 h of treatment with BSO in different concentrations. Mean values from five replicate experiments are shown

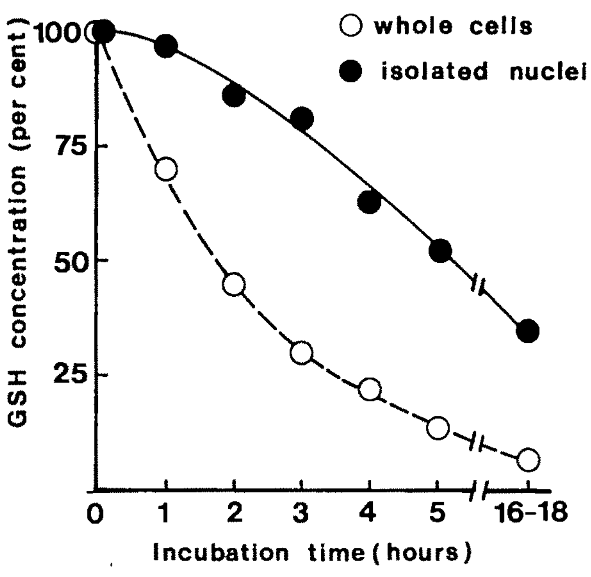

FIG. 2

The level of GSH in whole cells and corresponding isolated nuclei after treatment with 0.1 mM BSO for varying periods. Mean values from two to six replicate experiments are presented level after about 5 h of treatment (Fig. 2). Corresponding depletion from the whole cells occurs after only 2 h of treatment and about 90% is depleted after 5 h.

Since some leakage of GSH can be supposed to occur from the nuclei during the isolation procedure, the nuclear GSH values presented here are probably underestimated. Even with such underestimated values, our observations can be interpreted to indicate a compartmentalisation of GSH in the cells, and that the effect of BSO is different in the different compartments Determination of the GSH level in the whole cells may, therefore, not reflect the change in the amount of GSH at locations where it could be of importance in treatment. This consideration is supported by the finding that the effect of oxygen in enhancing the yield of DNA breaks, assumed to occur in competition with GSH, is related to the GSH content in the nucleus rather than to its content in the whole cell (Edgren, 1987) It is conceivable that the GSH-dependent effect of some DNA alkylating substances is similarly influenced specifically by the nuclear GSH This question is being investigated in current experiments.

Caution is suggested, therefore in indiscriminately using the GSH content of the whole cell when the effect is evaluated of a GSH-dependent treatment, confined to some specific location in the cell

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1987, *The British Journal of Radiology*, *60*, 725–726 JULY 1987

# Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

## Should aminophylline be used in acute bronchospasm induced by contrast media?

THE EDITOR—SIR,

Bronchospasm is a well recognised side-effect of intravenous contrast agents A degree of bronchospasm occurs in the majority of patients following such agents (Littner et al, 1977, 1981) and severe reactions to conventional media occur in one in 14000 investigations (Ansell, 1970) Bronchospasm is a prominent feature in about 12% of these cases of severe reactions and asthmatic patients are particularly susceptible; the reaction is not related to the dose of contrast medium (Ansell, 1970).

Newer contrast media such as iopamidol and iohexol are associated with a lower prevalence of bronchospasm (Dawson et al, 1983; Longstaff & Henson, 1985) although severe bronchospasm has been reported following the use of ioxaglate (Carty, 1983)

We contacted 14 major training radiology departments in the UK; in 12 of these the initial treatment of bronchospasm was oxygen administration and intravenous aminophylline (250 mg bolus, given slowly). This is in line with the recommendation in two current texts of radiological technique (Chapman et al, 1981; Whitehouse & Worthington, 1983).

Intravenous aminophylline can cause deaths (Bresnick et al, 1948, Camorata et al, 1971, Chaithiraphon, 1976) and should be used with caution in patients with heart disease, liver disease and in elderly patients (British National Formulary, 1986). Bolus injection of aminophylline in acute asthma in patients already taking methylxanthine preparations may raise the serum theophylline levels above the recommended therapeutic level (10–20 ng/l) (Stewart et al, 1984). Patients who do not have asthma and who develop bronchospasm following intravenous injection of contrast medium are also at risk. They are often elderly, infirm and suffer from cardiac ischaemia and impaired liver function. In these patients the clearance of aminophylline is impaired particularly if the patient becomes hypotensive (Powell et al, 1978). On the other hand, inhaled sympathomimetic agents produce more rapid and effective bronchodilatation than intravenous aminophylline (Rossing et al, 1980). The side-effects of inhaled $\beta$-agonists are rarely troublesome and there is no significant interaction with other drugs, including maintenance theophylline (White & Addis, 1983).

We would suggest that the first line in treatment of contrast-medium induced bronchospasm should be oxygen and nebulised or aerosol $\beta$-agonists, and that intravenous aminophylline should no longer be used.

Yours, etc.,
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(*Received December 1986 and in revised form January 1987*)

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## Invisible field skin-marking on radiotherapy patients

THE EDITOR—SIR,

Like R. E. Hutchings (1986), this department has found that patients prefer the anonymity of marking afforded by an ink which fluoresces under ultraviolet (UV) illumination.

In over 13 years since my technical note (Aves, 1973) was published, we have observed no adverse skin reaction in any patient.

Initially we too used mains-driven UV lamps, but found a change to battery-powered, hand-held lamps provided greater convenience. Such a lamp is the "Blak Ray" Mi5 manufactured by UV Products Ltd, Science Park, Cambridge

1987, *The British Journal of Radiology, 60*, 726–728

CB4 4BN. The nickel cadmium battery can be recharged overnight, and then gives illumination for about an hour, sufficient for several days' work. The lamp is fitted with a Woods filter and can be safely used close to the eyes, although many patients prefer to keep them closed

Yours, etc ,
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(*Received January 1987*)

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## Tissue analysis by dual-energy computed tomography

THE EDITOR—SIR,

In a recent paper, Hawkes et al (1986) suggest a method of characterising body tissues using hypothetical mixtures of water and calcium chloride They state that characterisations using electron density and effective atomic number are inaccurate and should be abandoned.

It is well recognised that there are inaccuracies involved in measuring the properties of internal organs using a computed tomography (CT) scanner These include statistical noise on the CT numbers, partial-volume effects, patient movement, the presence of image artefacts and uncertainty about the X-ray spectrum at the point of interest as a result of beam hardening. Despite the implication in the paper of Hawkes et al, that their method is immune to the latter, this is not so since their factor $\Phi_c$ is dependent on the X-ray spectrum and will therefore vary with position in the body They claim that in addition to these errors, there are fundamental inaccuracies in the effective atomic number (Z*) method which render it ineffective for tissue characterisation.

We have examined the accuracy of mass attenuation coefficient $\mu/\rho$ values predicted by the Z* method against values calculated by the method of mixtures for a range of tissues. The methods used are those already published (Henson, 1983, Henson & Fox, 1984) The mass attenuation coefficient for a mixture of elements representing a specific tissue is given by.

$$\frac{\mu(E)}{\rho} = \frac{10^{-24}N_0}{A^*} f(Z^*, E) \tag{1}$$

where $A^*$ is the mass number for the tissue and $N_0$ is Avogadro's number. The function $f(Z^*, E)$ has been defined by Henson (1983).

Z* may be calculated by considering the mass (or linear) attenuation coefficients for the material at two energies, $E_1$ and $E_2$.

$$\frac{\mu(E_1)}{\mu(E_2)} = \frac{f(Z^*, E_1)}{f(Z^*, E_2)} \tag{2}$$

Note that Z* is defined from the total linear attenuation coefficient and not just that of the photoelectric effect. There is, however, a small dependence of its value on the pair of energies used in its definition, although in practice this difference has negligible effects on the analysis.

$A^*$ may be derived from the relation

$$\rho_e = N_0 Z^* \rho / A^* \tag{3}$$

where $\rho_e$ is the electron density and $\rho$ is the mass density for unit volume

For a tissue consisting of a mixture of elements in known proportions by mass, it is possible to calculate accurately by the method of mixtures both the mass attenuation coefficient at any desired photon energy and the number of electrons per unit mass of material Equation (2) is used to calculate Z*, Equation (3) is used to calculate $A^*$ and, finally, Equation (1) enables the value of the mass attenuation coefficient to be calculated at the desired photon energy. These values can then be compared with those calculated directly using the method of mixtures.

Table I gives the percentage difference of these two values of mass attenuation coefficient for a range of tissues at a photon energy of 70 keV and the mean and standard deviation of the percentage differences for a range of energies from 40 keV to 140 keV The values were calculated using 50 keV and 100 keV as energies $E_1$ and $E_2$ in Equation (2). However, the results are not significantly altered at other choices for $E_1$ and $E_2$ between these two values

It is evident that this difference is always less than 1% over a wide range of energies for a range of relevant body tissues and in most cases is less than 0.5% Consequently there is no evidence that the method using an effective Z* is subject to intrinsic inaccuracies which are unacceptable for characterising body tissues Obviously identical results would have been obtained if we had compared calculated and "true" values of

TABLE I

PERCENTAGE DIFFERENCES BETWEEN $\mu/\rho$ VALUES CALCULATED USING THE METHOD OF MIXTURES AND THE EFFECTIVE ATOMIC NUMBER FOR VARIOUS TISSUES

| Tissue | Mean % difference* (40–140 keV) | Standard deviation of % difference | % difference* at 70 keV |
|---|---|---|---|
| Cortical bone† | −0.33 | 0.28 | −0.09 |
| Spongiosa† | 0.00 | 0.22 | 0.10 |
| Red marrow† | −0.20 | 0.26 | −0.34 |
| Yellow marrow† | −0.42 | 0.31 | −0.63 |
| Cartilage† | −0.05 | 0.22 | −0.15 |
| Fat‡ | −0.56 | 0.33 | −0.80 |
| Adipose‡ | −0.41 | 0.30 | −0.61 |
| Muscle‡ | −0.07 | 0.22 | −0.17 |
| Kidney‡ | −0.07 | 0.22 | −0.17 |
| Pancreas‡ | −0.07 | 0.22 | −0.18 |
| Brain‡ | −0.06 | 0.22 | −0.16 |

*% difference = 100 (mm-Z*)/mm where mm is the value of $\mu/\rho$ from the method of mixtures and Z* its value by that method Mean taken of energies at 1 keV intervals. The energy pair used to define Z* was 50 keV and 100 keV

†From Woodard and White (1982).

‡From the International Commission on Radiological Protection (ICRP) (1975)

electron density using known values of the linear attenuation coefficient, which is how Equations (1), (2) and (3) have previously been used with the CT scanner.

In view of the greater complexity of using Equations (1), (2) and (3) compared with the method of Hawkes et al, the value of using it may be questioned despite its accuracy. We believe that the ability to define a tissue by an electron density and an effective atomic number is of more value than using equivalent masses of water and calcium chloride There are a number of situations where an accurate determination of electron density for a tissue may be of value. Table I shows that, apart from the errors implicit in all CT measurements, electron densities with an accuracy of better than 1% should be obtainable.

Yours, etc ,
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P. HENSON

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(*Received December 1986*)

(*Authors' reply*)

THE EDITOR—SIR,

We thank Dr Fox and Mr Henson for their interest in our paper (Hawkes et al, 1986). We wish to reply to certain points raised in their letter

Our method can be used to derive the electron density of tissue. Our dual-energy technique defines a hypothetical mixture of water and a reference material. This mixture has the same linear attenuation coefficient as the tissue it represents over a wide energy range, from 30 keV to over 200 keV This mixture also has the same electron density (electrons per unit volume) (Hawkes, 1982) We have verified this result experimentally for 13 liquids with electron densities ranging from 20% below that of water to 20% above Cyclohexane and aqueous solutions of calcium chloride, potassium chloride or isopropyl alcohol were contained in polythene vials of internal diameter 25 mm, which were inserted into a cylindrical perspex phantom of diameter 320 mm. The phantom was scanned at 140 kVp and 87 kVp on an EMI CT5005 The water and calcium chloride coefficients, $m_w$ and $m_c$, were derived by the method described in our paper. The number of electrons per unit volume, the electron density $\rho_e$, is given by

$$\rho_e = \rho_w(m_w d_w + m_c d_c) \qquad (1)$$

where $d_w$ and $d_c$ are the number of electrons per unit mass of water and calcium chloride respectively and $\rho_w$ is the density of water The standard deviation of the differences between the electron densities calculated from the atomic composition of the liquids and the dual-energy estimates of the electron densities was 0.5%, which was consistent with estimates of the error due to uncertainties in the original CT data.

Concerning the use of effective Z or Z*, while it is true that the attenuation coefficient of a range of elements, over a restricted range of X-ray energies, can be fitted by expansions of the form described by Henson (1983) we feel that such equations give little insight to the significance of the underlying physical processes The extension of such expressions to mixtures, where the discrete variable Z is replaced by the continuous variable Z*, must be made with care. In particular, we have shown (Jackson & Hawkes, 1981) that Rutherford's formula (Rutherford et al, 1976) can lead to significant errors at the extremes of the photon energy and atomic number ranges encountered in CT Relating small changes in effective Z to small changes in the concentration of different tissue components (lipid, bone mineral, etc.) could lead to erroneous or misleading conclusions

Their simulation does not represent the complete dual-energy experiment They have performed their calculations at two discrete energies, rather than using a broad spectrum of X-ray energies In practice, the effective energies of the CT scanner must be measured under identical conditions to those of the scans of the patient. The dual-energy experiment is then used to derive the electron density and effective atomic number of the tissue. It is not obvious what effect errors in their representations of the linear attenuation coefficient would have on the accuracy of predictions of tissue composition.

We have derived an analytical formula for the attenuation coefficient (Jackson & Hawkes, 1981) from first principles, which we feel does provide some insight into the importance of the various underlying physical processes We have also developed a method for tissue analysis by dual-energy CT which is conceptually straightforward; the calibration is easily achieved and the analysis is simple to perform. The effect of any small errors in our representation of the attenuation coefficient is easy to predict.

Finally, it was asserted that we had implied that our method was immune to beam-hardening errors We feel that this conclusion could not be drawn from our paper The factor $\phi_c$, which is defined as 1000 times the ratio of the mass attenuation coefficients of calcium chloride and water integrated over the detected energy spectrum, is constant over the field of view if the detected energy spectrum is identical for all projections. Beam-hardening errors will occur if the detected energy spectrum varies The errors due to beam-hardening effects were discussed in some detail in the section headed "Accuracy of technique" in our paper.

Yours, etc.,
D. J. HAWKES
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(*Received December 1986*)

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## The position of the personal dosemeter in diagnostic X-ray practice

THE EDITOR—SIR,

When a lead apron is worn, the International Commission on Radiological Protection (ICRP) (1982) recommends that a personal dosemeter should be positioned outside the apron, usually high on the trunk. The reason given for this recommendation is that the dosemeter will then provide information on dose to much of the parts of the body not shielded by the apron.

A further reason for endorsing this recommendation arises from the effect of the high level of attenuation offered by a lead apron to diagnostic X-rays. This in combination with the fact that commonly used personal dosemeters have a minimum reporting level means that unacceptably high levels of dose could be incident on a lead apron and not be detected by a dosemeter positioned underneath.

Table I gives some values of attenuation factor for broad-beam transmission of X-rays through 0.33 mm lead, a thickness representative of lead aprons. Also given are the required levels of dose incident on the apron to enable the dose transmitted through the apron to reach the commonly used minimum reporting level of 0.1 mSv.

TABLE I

| kV | 50 | 75 | 100 |
|---|---|---|---|
| Attenuation factor | 1850 | 70 | 22 |
| Incident dose (mSv) required for a transmitted dose of 0.1 mSv | 185 | 7 | 2.2 |

Clearly, the high attenuation in the apron and the minimum reporting level combine to invalidate the function of a dosemeter positioned under the apron, except where the levels of incident dose are extremely and uncomfortably high.

Yours, etc.,
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(*Received January 1987*)

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## The non-ionic dimers, a new class of contrast agent

THE EDITOR—SIR,

I read with interest the paper by Dawson et al (1986) reviewing non-ionic dimers as contrast agents. However, I would like to add another possible clinical application to those they suggested. There is a definite need for reduction in contrast-mediated side-effects in endoscopic retrograde pancreatography (ERP). A recently published trial, with which I was involved, convincingly demonstrated that reduction in osmolality reduces the incidence of post-ERP clinical pancreatitis (Banerjee et al, 1986).

Although there are at present no published trials available of non-ionic dimers and ERP, a further reduction of osmolality of the contrast media may be postulated to have a further beneficial effect. Since ERP is being more widely practised, the use of non-ionic dimers in this procedure is perhaps another important potential clinical use of these agents.

Yours, etc.,
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(*Received January 1987*)

(*Author's reply*)

THE EDITOR—SIR,

A transient rise in serum amylase frequently follows ERP. It seems reasonable to assume that the hyperosmolality of the contrast agent used plays some role in this phenomenon. Studies such as that of Dr Banerjee and his colleagues (Banerjee et al, 1986) suggest that the newer agents with their lower osmolality may be safer in this regard. If this is so then, as Dr Banerjee suggests, the non-ionic dimers could be expected to be safer still since they are, at all concentrations, iso-osmolar with plasma. However, in order to establish this with certainty, large-scale studies would be needed, as the incidence of clinical pancreatitis following ERP, as opposed to hyperamylasaemia, is very low.

Yours, etc.,
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(*Received February 1987*)

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1987, *The British Journal of Radiology*, *60*, 729–731 JULY 1987

# Proceedings of The British Institute of Radiology

## Regulations and guidance on radiation protection

Abstracts of papers presented at the above meeting, held at the Edward Lewis Lecture Theatre, Windeyer Building, Middlesex Hospital Medical School, Cleveland/Howland Street, London W1, on Thursday, October 2, 1986

**Chairmen: Professor R. J. Berry and Mrs J. Barrett**

Training requirements in terms of current legislation, by J. R Gill
Practical training for radiation protection supervisors, by R G. C. Grix
Equipment acceptance, maintenance and modification, by I. R. F. Hendra
The protection of the patient with particular reference to ECC Directive 84/466 Euratom, by B E Godfrey
Diagnostic uses of ionising radiations, by P J. Richardson
Radiation protection requirements in a small radiotherapy unit, by B. D. Aves
Nuclear medicine, by L. K Harding
Medical uses of radiation outside the NHS hospital environment, by P. J Roberts
Cost benefit, by J. G B Russell

### TRAINING REQUIREMENTS IN TERMS OF CURRENT LEGISLATION

J. R. Gill

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Section 2 of the Health and Safety at Work (HSW) Act places a duty on every employer to ensure, so far as is reasonably practicable, the health, safety and welfare at work of all his employees. There is also a duty to prepare a written statement of his general policy for the health and safety at work of his employees and the organisation and arrangements for carrying out the policy, and the employer must bring that statement to the notice of all employees. The Health and Safety Executive (HSE) has published a guide to the HSW Act (HSE, 1980) which gives general ideas about the scope of the training requirements. In 1983, the Health Services Advisory Committee of the Health and Safety Commission (HSC) published a guidance booklet, *Safety Policies in the Health Service* (HSC, 1983). This contains a checklist of matters to be covered in the safety policy, and in this checklist are five questions to be asked about training.

(1) Is there a system for the identification of training needs?
(2) Is the responsibility for training properly allocated?
(3) Does training cover all levels, from senior manager to new entrant?
(4) Are special risks analysed for training requirements?
(5) Are refresher courses arranged?

Regulation 12 of the *Ionising Radiations Regulations 1985* deals with information, instruction and training. Employers must ensure that:

(a) employees working with ionising radiation receive information, instruction and training to enable them to work in accordance with the regulations;
(b) adequate information is given to other persons directly concerned with the work to ensure their health and safety so far as is reasonably practicable;
(c) classified persons and trainees are informed of the health hazard, if any, associated with their work, the precautions to be taken and the importance of complying with the medical and technical requirements and are given appropriate training in the field of radiation protection; and
(d) women engaged in work with ionising radiation are informed of the possible health hazard to the fetus in early pregnancy and of the importance of informing the employer as soon as they discover that they have become pregnant.

The *Approved Code of Practice* (HSC, 1985), giving guidance on Regulation 12, points out that the standard of training to be given to classified persons, trainees and radiation protection supervisors, should be appropriate to the nature of their work, and that the employer should consult the radiation protection adviser about training requirements.

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### PRACTICAL TRAINING FOR RADIATION PROTECTION SUPERVISORS

R. G. C. Grix

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Current training for radiation protection supervisors (RPSs) ranges from in-service courses to those offered by the National Radiological Protection Board (NRPB), selected educational establishments and private consultancies. Standards which will provide a common objective for this training, and which would provide better guidance to employers and regulatory bodies, have yet to be produced; but development of a promising co-operation between the Open University and the Institute of Radiation Protection could overcome problems caused by assessment, period of release, and the wide range of academic achievement of the RPSs. It is intended that this development would supplement present courses.

Different applications could be categorised as those of the nuclear operators, the public services (particularly health and education), and industry Despite their apparent differences, there are fundamental precepts and areas of knowledge that every RPS will need to acquire. Examples are given below.

(1) The physical and biological background to radiation protection
(2) The meaning and the dimensions of the units used
(3) Sufficient awareness of relevant legislation and guidance for day-to-day operation and for any likely circumstance.
(4) A basic understanding of the performance and limitations of instruments used for radiation protection and the techniques of using them for an appropriate operation

(5) Some ability to assess radiation exposure for prediction of control and for retrospective investigation
(6) An understanding of the way to influence those whom they are protecting and those who provide the resources.
(7) An ability to assess an untoward situation and to know when and where to get external assistance.

Additionally, RPSs in the health services need a heightened awareness of radiation exposure, since the medical use of radiation is unique in that it deliberately exposes people in the course of normal practice.

### EQUIPMENT ACCEPTANCE, MAINTENANCE AND MODIFICATION

I. R. F. Hendra

*DHSS Technical Branch, London*

The issues of equipment acceptance, maintenance and modification are addressed only in broad terms in the *Ionising Radiations Regulations 1985*. No information is given concerning the manner in which compliance may be achieved. The view is expressed that the practical issues in these areas are largely determined by the efficacy of the procedures used in the procurement of goods and services. This is an area in which the Scientific and Technical Branch of the NHS Procurement Directorate has been involved for many years. The significance of both the DHSS Manufacturer Registration Scheme and the Technical Requirements of the National Contract are explained in the context of equipment acceptance. A DHSS "Blue-cover" report on the maintenance of equipment is described in the form of a precedent, and a comment is included about the need for communication with users after equipment has been modified

### THE PROTECTION OF THE PATIENT WITH PARTICULAR REFERENCE TO ECC DIRECTIVE 84/466 EURATOM

B. E. Godfrey

*DHSS, London*

An historical outline of the development of the ECC Directive over the period 1973–84 provides the background against which its implementation can be viewed The Articles of the Directive and the proposals for regulatory implementation are reviewed. Specific attention is given to proposals which are still under consideration

### DIAGNOSTIC USES OF IONISING RADIATIONS

P. J. Richardson

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Following consultation and discussion on the *Regulations*, *Approved Code of Practice*, and *Guidance Notes* the time has arrived for the profession and practitioners to proceed with implementation The presentation attempts to promote practical solutions to the challenges of the *Regulations* and suggests their introduction to the X-ray imaging department. The planning and positioning of controlled areas are discussed together with appropriate warning signs The protective measures necessary for mobile and theatre radiography are outlined A model set of local rules detailing the access to controlled areas is presented. Brief mention is made of training needs, worker classification, problems associated with the extended working day and schemes of work.

### RADIATION PROTECTION REQUIREMENTS IN A SMALL RADIOTHERAPY UNIT

B. D Aves

*Radiotherapy Department, Pembury Hospital, Kent*

The new requirements for radiation protection of the *Ionising Radiation Regulations, Approved Code of Practice*, and *Notes for Guidance*, are considered in relation to a small radiotherapy department. Local rules and schemes of work to be written must define the controlled and supervised areas Decisions must be taken as to whether certain workers should be defined as classified or non-classified, both groups requiring regular monitoring. Contingency plans must be available in each work area (such as cobalt-therapy treatment rooms) to guide staff in restricting radiation doses received when dealing with foreseeable accidents, such as a stuck cobalt source. The duties and responsibilities of the Radiation Protection Supervisor are defined

### NUCLEAR MEDICINE

L. K. Harding

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The practice of nuclear medicine requires integration of radiation safety with patient care, and radiopharmaceutical standards Nationally there was useful discussion before the *Ionising Radiations Regulations* and *Approved Code of Practice* were published, although such consultation had been lacking when the Medicines Act was imposed. Most of the new considerations relating to nuclear medicine stem from Schedule 6 of the *Regulations*. Generally the presence of a single patient does not require a controlled area. However, when several patients are present, or radiopharmaceuticals are being prepared prior to injection, a controlled area will be required Classification of workers is not likely to be required in a typical nuclear medicine department in the UK, although most parts of the nuclear medicine department will need to be controlled areas These include the radiopharmacy, radionuclide dispensary, injection room and imaging rooms if patients are injected in them. The importance of finger dose measurements is emphasised. Patient wards, however, need not be controlled areas.

A particular concern in nuclear medicine was that patients should not need to be admitted to hospital merely to comply with the legislation This is possibly the case and clarification will probably be available when the *Notes for Guidance* are published. Most procedures in nuclear medicine departments will remain unchanged. Further information is required, however, on patient waiting rooms, handling flood sources, pregnancy, and breast feeding Within the hospital, detailed and multidisciplinary discussion will need to take place within the forum of the radiation safety committee

### MEDICAL USES OF RADIATION OUTSIDE THE NHS HOSPITAL ENVIRONMENT

P. J Roberts

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The use of radiation in medicine extends outside NHS hospitals to private hospitals, medical schools, dental clinics, private practices, domiciliary radiography and veterinary clinics. The *Ionising Radiations Regulations 1985, Approved Code of Practice* and *Notes for Guidance in Medicine* apply equally to these situations. The range of radiation work in private hospitals is the same as within the NHS Local rules and systems of work are used to enable personnel to enter controlled areas without personal classification In general, if work load is limited, the controlled area in a dental clinic is also limited. Only simple local rules and cautionary notices are needed Only 1% of dental clinic staff in the West Midlands in 1985 and 1986 received measurable doses The same protection criteria apply to private and State dental practices In 1985, 5% of staff had measurable doses, whereas in 1986 the figure is only 3% so far. No-one has exceeded an annual total or pro rata annual total of 5 mSv. The draft guidance notes incorporate protective measures for the patient which are of greater consequence for population dose.

The problems in veterinary practices are similar to those for mobile X-ray equipment. The Health and Safety Executive has recognised this and defined controlled areas for veterinary radiography under certain stringent conditions. If no-one enters this controlled area, no radiation protection adviser is needed. In general, the safest procedure is to anaesthetise the animal so that no-one need be close to it. In the West Midlands, less than 2% of veterinary staff monitored in 1985 and 1986 received measurable doses There seems to be no cause for alarm concerning staff doses in veterinary radiography practice In conclusion, there appear to have been no serious problems in implementing the *Regulations* for medical practices outside the NHS.

### COST BENEFIT

J. G. B. Russell

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To be cost effective, a method of radiation protection must cost less than the value of the detriment of the population radiation dose it saves. The unit to which changes are made is the X-ray room The value of the detriment saved is obtained from the formula. (initial population dose, man-Sv) × (% saving available) × (value of the detriment, £/man-Sv) The initial population radiation dose of an X-ray room can be obtained by determining the work load of the room in respect of the number and type of examinations and multiplying the result by the average effective dose equivalent for each examination (Russell & Wrigley, 1986). The percentage savings available for several methods of protection have been indicated (Hufton & Russell, 1985) A suggested value of the detriment for medical work, derived from advice given by the National Radiological Protection Board (1986), is about £6000/man-Sv for the exposures to patients The annual doses to staff, which are lower in general than those to patients, call for a lower value, *e.g.* £3000

Comparison of the cost of methods of protection and the value of the saving of the detriment is made. It is found that reducing radiation exposure of the patient by the use of rare-earth screens and by introducing low-attenuation materials into the primary beam after it has left the patient are highly cost effective (Russell, 1986). Reducing staff dose is not, in general, cost effective, but a consequence of reducing patient radiation dose is a proportional reduction in staff radiation dose

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# Diagnostic and therapeutic uses of radioisotopes in oncology

Abstracts of papers presented at the above meeting of the Nuclear Medicine Subcommittee, held at Institute House, 36 Portland Place, London W1N 4AT on Wednesday, November 26, 1986

**Chairmen: Professor R. J. Berry and Dr K. E. Britton**

The role of the bone scan in carcinoma of the breast, by I. Fogelman
Strontium-89 therapy for skeletal metastases, by A. H. Laing
Uses of MIBG in chromaffin tumours, by M. Fischer
Imaging of bronchial carcinoma using technetium-glucoheptonate, by N. Garvie
Tumour imaging using labelled monoclonal antibodies, by M. Granowska and K. E. Britton
Regional antibody therapy, by A A Epenetos
Radionuclide imaging in medullary carcinoma of the thyroid, by S. E M. Clarke
The uses of iodine 131 in the management of thyroid carcinoma, by P. N. Plowman
Technetium-99m HMPAO for the detection of tumours and measurement of blood flow, by V. R McCready, D. Tate, F. Keeling, P A G. Hammersley, T. Davidson, R. J Ott, J Babich and M Flower

### THE ROLE OF THE BONE SCAN IN CARCINOMA OF THE BREAST

Ignac Fogelman

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While it is generally accepted that radionuclide bone scanning is the most sensitive investigation for detecting skeletal metastases, considerable controversy exists over its role in the evaluation of patients with clinically early breast cancer and no bony symptoms This has arisen because of wide discrepancies in the reported rates of abnormal bone scans in early breast cancer, with values for clinical Stage I ranging between 0% and 18% (mean value 4 4%) and in Stage II between 0% and 32% (mean value 7.2%) The reason for these varying results is not apparent While the bone scan is, indeed, sensitive, scan findings are non-specific and it is essential to confirm the significance of bone scan abnormalities by other, more specific, techniques If radiographs of the area in question are normal, then this would support the presence of a metastasis. If clinically relevant, a computed tomographic scan or biopsy may be indicated The frequency of abnormal bone scans at presentation in patients with more advanced breast cancer is generally accepted to be higher, with values for Stage III in the region of 28%.

The role of serial bone scan imaging is more controversial, with results from various centres again showing considerable discrepancy Pick-up rates of between 10% and 26% have been reported, with 2-year follow-up However, it is apparent from such studies that the bone scan will identify metastases before radiography with a lead time of between 0 and 17 months (mean 4 months). It has been shown that a positive bone scan is a serious prognostic factor, with patients having a marked increase in mortality when compared with those with normal bone scans The bone scan may, in addition, be of value in assessing the response of metastases to systemic therapy. However, it is apparent that a "flare" may occur with successful therapy, and bone scans obtained within the first 6 months can show apparent deterioration, with new lesions visualised

In view of the conflicting data in the literature, it is hardly surprising that there is no overall consensus with regard to the role of bone scanning in breast cancer. It is generally accepted that a bone scan should be obtained in patients with symptoms such as bone pain, soft-tissue metastases and locally advanced disease for prognostic purposes A bone scan at presentation is useful as a baseline for later comparison, and is mandatory for all patients being entered into therapeutic trials, to assess the adequacy of randomisation of patients.

## STRONTIUM-89 THERAPY FOR SKELETAL METASTASES

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Strontium 89 has been used in the treatment of skeletal metastases since the early 1970s In 1984 a number of centres in Britain started a prospective study in patients with multiple bony metastases from carcinoma of breast and prostate for whom conventional therapy had failed It was planned to study the biodistribution, and to produce a dose–response curve using doses of strontium between 40 and 80 $\mu$ Ci kg$^{-1}$. A "score" was produced to estimate response using four factors quality of life, mobility, analgesics required, and level of pain The work on biodistribution carried out at Southampton has shown, in patients with a few metastases, good correlation of whole-body retention of strontium 89 with the ICRP curve. However, in patients with extensive disease the retention in the body has been greater with a much longer half-life. Spiking the strontium 89 with strontium 85 has shown that this is because of the longer retention in the metastases compared with that in bone marrow It has also been shown in those patients that there is depressed urinary excretion of strontium. These factors have led to absorbed doses in individual vertebral metastases of between 3700 and 18 200 cGy and to a ratio of absorbed dose between bone marrow and metastases of between 8 and 10 to 1. The major toxicity of the treatment has been bone marrow depression, especially in patients with extensive replacement of marrow with metastases. The nadir has tended to be lower with larger doses of strontium

As yet there is no clear trend in the dose–response curve Of 36 patients with carcinoma of the prostate who were assessable at 12 weeks, three showed no benefit, eight some improvement, 16 substantial improvement and nine dramatic improvement. Of six patients with carcinoma of breast assessed at 12 weeks, two showed no benefit, two some improvement and two substantial improvement. The duration of response was variable, averaging about 20 weeks, and retreatment was usually effective

## USES OF MIBG IN CHROMAFFIN TUMOURS

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Between 1981 and 1986 about 250 patients with suspicion of chromaffin tumours were studied by scintigraphy with $^{123}$I- or $^{131}$I-labelled metaiodobenzylguanidine (MIBG) In 42 of 44 patients with phaeochromocytoma, confirmed by surgery and/or biochemically, scintigraphy localised the lesion(s) correctly In two of 44 patients (one intra- and one extra-adrenal tumour) scintigraphy was false negative. Of 17 children with neuroblastoma, MIBG scintigraphy was true positive in 13, false negative in one and true negative in three children in full remission Six patients with carcinoid tumours underwent MIBG scintigraphy. Scintigraphic imaging was true positive in four of the six, but false negative in two Six patients with phaeochromocytoma and three children with Stage IV neuroblastoma were treated with single doses of 65–210 mCi $^{131}$I-MIBG up to total doses of 200–1300 mCi. In conclusion, scintigraphy with $^{123}$I- or $^{131}$I-MIBG is effective in localising chromaffin tumours, especially small intra-adrenal, extra-adrenal and multilocular lesions, as well as bone marrow infiltration in children with neuroblastoma. Because computed tomography may fail to image these lesions, MIBG scintigraphy should be the first choice of imaging modality, especially in monitoring children with chromaffin tumours and those patients in whom the diagnosis of phaeochromocytoma was made during childhood, because about 69% of recurrences in these patients are malignant. In all patients treated with $^{131}$I-MIBG we observed an improvement of clinical symptoms after the first therapeutic doses, but four of six patients with a phaeochromocytoma and all children with neuroblastoma died from tumour progression In two patients with malignant phaeochromocytoma an increase in tracer uptake was observed after chemotherapy. During an oncological meeting in Rome (September 1986) some groups reported on $^{131}$I-MIBG therapy in 76 children with neuroblastoma. In 26, complete or partial remission was observed. The number of patients with phaeochromocytoma, neuroblastoma and other chromaffin tumours treated with $^{131}$I-MIBG is small. In most patients no curative effect was observed, but improvement or stabilisation of clinical symptoms and, in some children with neuroblastoma, full remission may be reached by combination of different therapeutic modalities (surgery, chemotherapy and MIBG-treatment).

## IMAGING OF BRONCHIAL CARCINOMA USING TECHNETIUM-GLUCOHEPTONATE

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The glucoheptonate molecule is chemically closely similar to that of glucose, and it is conceivable, therefore, that its uptake in various structures is related to metabolic activity, in particular to glycolysis. This metabolic pathway is favoured by certain tumours, particularly under anaerobic conditions, and the role of this agent as a potential agent for imaging carcinoma of the lung is described.

One hundred and eleven patients, referred for bronchoscopy with a clinical suspicion of lung carcinoma, were scanned using technetium-glucoheptonate (TcGh) Images were obtained 5 h after intravenous injection of 555 MBq and interpreted without knowledge of the clinical/bronchoscopic findings A positive histological or cytological diagnosis was obtained in each patient Sixty-four of the patients (58%) were subsequently shown to have carcinoma of the bronchus, the scan being positive in 43 (67%) of this group Uptake was also seen in several non-neoplastic pulmonary conditions, including pneumonia (six out of 14), sarcoidosis (three of seven), metastatic carcinoma (three of four) and bronchiectasis (two of four). Uptake associated with these non-neoplastic disorders was generally minor and diffuse, and usually distinguishable in terms of pattern appearance from tumour uptake The sensitivity of TcGh uptake as an index of malignancy was 68%, and the specificity 71% If, however, low-order diffuse uptake was eliminated, specificity rose to 95%, with a sensitivity of 63% The principal difficulty with this technique is the persistence of relatively high background levels, even at 5 h Further studies, involving subtraction of the blood pool activity using the equilibrium phase image after TcGh injection or a separate *in-vivo* technetium label, show considerable promise

## TUMOUR IMAGING USING LABELLED MONOCLONAL ANTIBODIES

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Radioimmunoscintigraphy is a complex imaging technique which requires the following: a tumour-associated or specific antigen to which a monoclonal antibody of high avidity and specificity can be made; radiolabelling of the antibody or the active fragment of it with a radionuclide whose half-life is appropriate to the kinetics of the antibody uptake by tumour; and detailed and serial imaging of the distribution of the intravenously injected compound. Interpretation of the images may be aided by computer-assisted analysis. General factors such as the tumour's blood supply, capillary permeability, size, composition and environment are important in determining the degree of uptake Radioimmunoscintigraphy takes advantage of specific features such as the expression and density of the tumour antigen. We have shown in colorectal cancer that this depends in turn on the degree of differentiation of the tumour. The presence of other disease, such as Crohn's, competes for antibody and reduces tumour uptake In the special case of using a radiolabelled monoclonal antibody against carcinoembryonic antigen (CEA), uptake by normal lymph nodes is much greater than that by locally involved nodes, which is presumed in the normal to be because of more efficient trapping of CEA, which is liberated into lymphatics when the basement membrane is broken by tumour. Improvements in image data analysis include subtracting the earlier image from the later ones and kinetic analysis with probability mapping (Granowska et al, 1986) Radioimmunoscintigraphy is currently being employed in the assessment of 14 different malignancies and its clinical indications are being worked out. Its main role is in the evaluation of the effects of treatment and the diagnosis of recurrence and not in primary diagnosis of cancer.

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## REGIONAL ANTIBODY THERAPY

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Following the demonstration (Epenetos et al, 1984) that monoclonal antibody targeted radiotherapy may prove a valuable form of treatment in certain situations, at least when it is delivered into body cavities and regions rather than intravenously, we expanded our studies in various areas.

(1) A randomised multicentre clinical trial using radioactively labelled monoclonal antibodies for the treatment of Stage III minimal residual disease ovarian cancer has recently been initiated, following the completion of a Phase I–II study where data were obtained regarding toxicity and response (2) Following the completion of a trial involving intracavitary administration of antibodies in the treatment of serous effusion (12 responders out of 15 patients), a randomised study has commenced of $^{131}$I-labelled specific versus non-specific antibody administered on an outpatient basis. (3) Six patients with Grade III/IV glioma, having relapsed after radiotherapy with or without chemotherapy, have received intra-arterial infusions of $^{131}$I-labelled monoclonal antibody (EGFRI, against epidermal growth factor receptor) Four out of six patients responded favourably with clinical and radiological improvement. (4) Monoclonal antibodies to carcinoembryonic antigen were radiolabelled with $^{131}$I and administered intra-arterially (via the hepatic artery) concurrently with biodegradable starch microspheres in order to enhance tumour uptake of antibody and achieve a therapeutic response. Favourable results were observed in one patient treated thus far A pilot study has recently commenced examining the potential therapeutic effect of this approach in patients with small ($<$ 2 cm diameter) liver metastases.

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## RADIONUCLIDE IMAGING IN MEDULLARY CARCINOMA OF THE THYROID

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Medullary carcinoma of the thyroid (MCT) is an uncommon tumour accounting for 10% of thyroid malignancies. Patients, however, survive many years following initial diagnosis, despite metastases Interest has been shown recently in two new radiopharmaceuticals, $^{131}$I metaiodobenzylguanidine (MIBG) and $^{99}$Tc$^{m}$ (V) dimercaptosuccinic acid (DMSA), which have been demonstrated to accumulate in sites of MCT We have evaluated the uptake of these two agents in patients with histologically proven MCT in an attempt to identify the role of each in the management of patients with MCT.

Ten patients (three male, seven female) with MCT, one with primary disease, the remainder with elevated serum calcitonin levels following thyroidectomy, were imaged 24 h and 48 h after administration of 1 mCi (37 MBq) of intravenous $^{131}$I MIBG. Uptake was seen in four patients, one with primary disease, three with metastatic disease. One patient with known pulmonary metastases had equivocal uptake in the lung fields. The remaining five patients had no uptake, despite proven metastases. Twelve patients (four male, eight female) with MCT were imaged using 10 mCi (370 MBq) $^{99}$Tc$^{m}$(V)DMSA Scans were performed 2 h after intravenous injection and uptake in sites of primary and recurrent disease was seen in nine of the patients imaged Three negative scans were obtained. Two of these were in patients who had had initial surgery and had normal calcitonin levels and no other evidence of recurrent disease The third negative scan was obtained in an asymptomatic patient with moderately elevated calcitonin levels after thyroidectomy, but no other evidence of recurrent disease Technetium-99m (V) DMSA has, therefore, successfully identified metastases in bone, liver and lung, producing excellent images It has a role in primary diagnosis and follow-up to assess recurrence and the success of therapy Iodine-131 MIBG, because of its high false negative rate, has no role in primary imaging, but its therapeutic potential in patients with uptake in known disease requires further evaluation

## THE USES OF IODINE 131 IN THE MANAGEMENT OF THYROID CARCINOMA

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Radioiodine ($^{131}$I) has a role in the management of follicular-cell origin (papillary and follicular) carcinomas of the thyroid. Following radical thyroidectomy, a dose of $^{131}$I (usually 3 GBq) is given to ablate the normal thyroid remnant before the patient is placed on thyroid-stimulating hormone (TSH) suppressive, replacement doses of liothyronine ($T_3$) There are now considerable amounts of data to support this practice of routine $^{131}$I ablation for both papillary and follicular carcinomas because high-avidity iodine-concentrating tissue and normal thyroid tissue with carcinogenic potential are both eliminated as well as, perhaps, local tumour However, for cases with a good prognosis, young patients (less than 35 years) with intrathyroidal papillary or small intrathyroidal microangioinvasive follicular growths, routine ablation with $^{131}$I is not routinely recommended. Children require similar management (Tubiana et al, 1985) Three months following the ablative dose of $^{131}$I and 8 days of $T_3$, with the endogenous TSH level high (more than 30 IU/l), a whole-body $^{131}$I profile scan is performed to seek low-avidity iodine-concentrating tumour recurrences Negative cases return to the screening programme (Plowman, 1986) Residual uptake in the thyroid bed is often due to incomplete ablation and may argue for a higher ablative dose Patients with tumour recurrences concentrating $^{131}$I receive therapeutic doses (usually 5 6 GBq) repeated at 3-monthly intervals until functioning tumour disappears, bone marrow tolerance supervenes or until six doses have been given. The dose received by the tumour depends on the activity administered, the avidity of uptake, the flux time and the tumour mass Iodine-131 therapy palliates patients with high-bulk disease and may cure those with low-bulk disease, usually in lungs (Brown et al, 1984). The risks of $^{131}$I usage in thyroid carcinoma management are quantifiable but small (Edmonds & Smith, 1986).

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## TECHNETIUM-99M HMPAO FOR THE DETECTION OF TUMOURS AND MEASUREMENT OF BLOOD FLOW

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The perfusion of human tumours is likely to play a major part in the uptake of drugs both for diagnosis and therapy Perfusion is also likely to determine the oxygenation and, therefore, the radiosensitivity of malignant tumours Technetium-99m HMPAO uptake has been studied in an animal model and in a variety of primary and secondary tumours A rabbit isolated hind limb preparation containing a VX sarcoma was used to measure the pattern of excretion of HMPAO and its relation to the uptake of $^{86}$Rb. A linear relation between the uptake of both agents was found in muscle, pieces of tumour and metastases Similar results were found following intravenous injection of both agents in a mouse model containing a subcutaneous transplanted tumour The extraction efficiency for HMPAO in saline was greater than 80% and for $^{86}$Rb between 40% and 50% In human tumours the pattern of perfusion in a variety of lesions showed a high-activity ring surrounding a low-activity centre Seven of seven lung tumours showed high uptake. Variable levels of uptake were seen in breast tumours (six), squamous-cell carcinoma (one), melanoma (one), sarcomas (three) and lymphomas (seven) Particularly clear definition of high uptake was seen in neck nodes involved by lymphomas The brain tumours studied usually demonstrated a return to normal perfusion in patients who improved clinically during radiotherapy This was most obvious in patients with metastatic disease. These initial results indicate a useful place for HMPAO in the detection of tumours in the thorax, and in imaging perfusion patterns in primary and secondary tumours It is hoped that this information will help predict the likely response to therapy

# BIR Bulletin

July 1987

## The 1987 BIR award winners

### Dr John L. Haybittle (Barclay Medal)

This year's Barclay Medal is awarded to Dr J. L. Haybittle for his contributions to the *British Journal of Radiology* over more than 30 years, encompassing physical techniques and dosimetry of photon and electron therapy, and the design and statistical analysis of clinical cancer trials.

John Haybittle read mathematics at St Catherine's College, Cambridge, in 1940, beginning a long association with that town, but his studies were interrupted by service in the Royal Air Force and when he returned it was to take a natural sciences degree in physics. He taught physics for a time at Norwich, but soon returned to Cambridge to join the Medical Physics Department at Addenbrooke's Hospital and became closely associated with the brilliant (although quixotic) Regius Professor of Physic, the radiotherapist Joe Mitchell. John prospered at Addenbrooke's, publishing 27 papers in the *BJR* during the period 1953–84, of which about half were devoted to radiotherapy physics and the majority of the rest to clinical trial design and statistical analysis. He was much involved in the design and calibration of the strontium unit for total-skin electron irradiation, a bold step at a time when whole-body irradiation with high-energy electrons from linear accelerators was a longed-for pipe-dream. In 1971 he became Chief Physicist at Addenbrooke's. He received the Röntgen Prize of the British Institute of Radiology in 1972 for his outstanding contributions to the Journal, but many of his greatest works were still to come. His analysis of the Kings/Cambridge Trial for Treatment of Early Breast Cancer was a model of how these things should be done, and reading his practical approach to the design of clinical studies is still an undisputed "must" for all radiation oncologists. A generation of young radiotherapists will long remember his lucid and humorous teaching of medical statistics in the F.R.C.R. Part I course.

John Haybittle became Honorary Editor of the *BJR* in 1981, but despite his exemplary services in that role, it is as an outstanding contributor to the Journal by his wide-ranging scientific output that his achievements are recognised by the award of the Barclay Medal.

R. J. BERRY

The presentations to the award winners at the Conversazione. From left to right: Dr John Haybittle, Professor Roger Berry (President), Dr Janet Husband and Professor William Duncan.

### Dr Janet Husband (Barclay Prize)

Dr Husband was educated at Headington School, Oxford, and trained in medicine at Guy's. After a spell in general practice she returned to Guy's as a lecturer in the physiology department. After obtaining her Membership she started her training in 1971 in the X-ray Department at Guy's, and completed her training in the department at King's College Hospital. In 1976, she was appointed Research Fellow at the Clinical Research Centre, Northwick Park Hospital, where she worked for one year with Dr Kreel on the first EMI whole-body scanner. A year later she was appointed as Research Fellow in the Computed Tomography Scanning Unit at the Royal Marsden Hospital, Surrey Branch, where in 1980 she was appointed as Consultant Radiologist. In 1985 she became Consultant-in-Charge of the department which now entails responsibility for a magnetic resonance unit. She is currently Director of the Cancer Research Campaign Radiological Research Group.

Dr Husband has an international reputation in the field of computed tomography (CT). She has published extensively on the subject, including authorship of a most successful textbook. She is in wide demand as a lecturer, both in this country and abroad. Her special interest is in the role of CT in the management of malignant disease. She is a member of the World Health Organisation Research Group advising on imaging.

Dr Husband has been a staunch supporter of the Institute and was Honorary Secretary from 1981 to 1984.

I. KELSEY FRY

(cont.)

**Professor William Duncan (Röntgen Prize)**

Bill Duncan graduated from Aberdeen University where he had already shown his qualities of leadership, having been President of the University Union. However, after completing his early clinical appointments at Aberdeen Royal Infirmary he left his native Scotland to undertake training in radiotherapy at the Christie Hospital in Manchester. He was appointed Consultant Radiotherapist at the Christie Hospital in 1964 and it was at this time that he first became interested in the potential of fast neutron therapy in the treatment of cancer

In 1971 he was appointed Professor of Radiotherapy at the University of Edinburgh and began the task of building up an academic radiotherapy unit. One of his principal hopes was that he would be able to establish a series of clinical trials to investigate fast neutron therapy. He believed that Edinburgh offered unique opportunities for the conduct of such studies His hopes were realised in 1975 with the setting up of the Medical Research Council Cyclotron Unit in Edinburgh In the following years, even though he fulfilled a heavy clinical and university commitment, he devoted himself to an intensive programme of research into fast neutron therapy.

He has subsequently received many awards in recognition of his international reputation He was awarded the MacKenzie Davidson Medal by the BIR in 1977 and was made Rohan Williams Professor of the Royal College of Radiologists in 1981 The Royal College of Surgeons of Edinburgh awarded him the Diploma of Fellowship without examination in 1977 and the American College of Radiologists awarded him honorary fellowship in 1982

He has had a great interest in both undergraduate and postgraduate education and persuaded Edinburgh University that the Radiotherapy Department had the potential to offer a substantial contribution to undergraduate education both in the general teaching of clinical examination and history taking, as well as oncology He served on the Education Board of the Royal College of Radiologists between 1971 and 1976 and was a member of the Examination Board between 1979 and 1982 He served as a member of Council and as Chairman of the Standing Scottish Committee of the Royal College of Radiologists He has also been a member of many committees of the Medical Research Council and was Chairman of the Working Party on Urological Cancer and on Rectal Cancer

William Duncan also made a considerable contribution to oncology in the international sense He was Chairman of the International Commission on Radiological Protection between 1980 and 1981 and was Chairman of the EORTC High LET Therapy Project Group from 1978 to 1981 He also served on the Executive Committees of the International Society for Radiation Oncology and the European Society for Therapeutic Radiology and Oncology and was Secretary General of the Third European Congress of Radiology, held in Edinburgh the organising skills which he demonstrated at that time will long be remembered

Professor Duncan has always been progressive in his views and this is no better exemplified than by his success in creating a unified department of clinical oncology in Edinburgh in 1980 following the appointment of Professor John Smyth as Professor of Medical Oncology. It is a great loss to British radiotherapy yet at the same time a great tribute to his abilities that in 1985 he was appointed Chief of Radiation Oncology to the Princess Margaret Hospital in Toronto.

S J. Arnott

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# BIR sponsored visit

## Interstitial curietherapy at the Institut Gustave-Roussy, 1985

Report of a 3-month elective period, October–December, 1985

By Anne Hong

The Institut Gustave-Roussy (IGR) is situated in the suburb of Villejuif, 3 km south of Paris and is one of 20 major French anticancer centres Completed in 1980, this 440-bed, purpose-built, 15-storey institute bears the name of Professor Gustave Roussy, co-founder and Physician-in-Charge of the first Institut du Cancer. It is a multidisciplinary centre and receives referrals not only from France, but also the rest of Europe and North Africa. There are an additional 164 non-acute beds at the IGR (La Grange), 35 km south of Villejuif

New patients are reviewed in combined clinics by a multidisciplinary committee and the treatment plan is decided jointly. The Radiotherapy Department treats 4000–5000 new patients per annum and is equipped with two linear accelerators (20 MV producing 6–19 MeV electrons and 25 MV producing 8–32 MeV electrons), five cobalt units, seven curietrons, three simulators and orthovoltage and superficial X-ray machines A third linear accelerator is currently being installed The department also possesses two radio-frequency resistive hyperthermia machines (0 5 MHz)

*Techniques*

Curietherapy is continuous low-dose-rate irradiation which delivers a high total dose to a limited volume, sparing normal tissue It is used as primary definitive treatment, as a supplement to external beam therapy or as a complement to surgery. Tumours amenable to this method of treatment must therefore be accessible, of moderate size and possess definable margins

The ideal source material should be small enough to be introduced into carrier systems, pliable both for patient comfort and to conform to anatomical and tumour contours, adaptable to afterloading systems for personnel protection and of reasonable cost Iridium 192, with a half-life of 74 days, average $\gamma$-ray energy of 0 35 MeV and diameter 0 3 mm or 0.5 mm, fulfils these criteria and is the most commonly used radionuclide at the IGR

Implants are planned using the Paris system of dosimetry (Marinello et al, 1978, 1979, Dutreix et al, 1982, Gillin et al, 1984) There are several steps in the afterloading procedure First the non-radioactive source-carriers or guides are implanted into the target volume Their position is then verified and provisional dosimetry is carried out They are then loaded with the active source(s) and definitive dosimetry is done Five carrier systems are used for interstitial curietherapy at the IGR plastic tubes, guide gutters, hypodermic needles, silk sutures and guide needles on a template For intracavitary curietherapy in gynaecological and nasopharyngeal tumours, individually made moulds are used to carry the sources (Pierquin & Marinello, 1981)

The operating suite is adjacent to the 30-bed Curietherapy Ward and is equipped with a mobile X-ray unit and image intensifier for screening the implant The operating table can be adjusted to take patients supine or sitting upright. Performing an implant on a sitting patient has the advantage, in head and neck tumours, of maintaining the normal position of anatomical structures, tissue tone and source position. The radionuclide bench is in a room adjacent to the operating suite so that the prepared sources can be passed quickly through a hatch for loading.

Plastic tubes (Pernot, 1982) are flexible and versatile, and are used for large and medium-sized tumours of skin, head and neck, breast, soft tissue, bladder, prostate and female pelvis Appropriate lengths of tubing, of external diameter 1.6 mm and internal diameter 1 2 mm, are cut as required depending on target volume Hollow stainless-steel needles (straight or curved) are implanted according to the desired distribution, and a nylon guide wire is threaded through The rigid needles can then be removed, leaving in place the nylon wire over which the plastic tube is drawn into position and fixed in place. The tubes can then be loaded

This technique has been adapted for a variety of sites and for special cases, such as paediatric tumours (Gerbaulet et al, 1985), per-operative curietherapy (bladder and prostate) and thermoradiotherapy For the latter, special metal and plastic tubes are used for combining hyperthermia with curietherapy. The metal mid-portion of the tube conducts heat while the plastic extremities act as a perfect insulator, sparing skin. Thermocouples can be introduced into the tubes for temperature measurement and, once hyperthermia is complete, iridium wires can be inserted

Guide gutters (Marinello et al, 1985) are used for small and medium-sized tumours of the oral cavity, nasal septum, vagina and urethra. The guide material is rigid, unlike plastic tubes. There are two types. single, for single hairpins, and double, with two parallel arms 3–5 cm in length and a bridge 1.2 cm wide, suitable for double iridium hairpins

Hypodermic needles (Daly et al, 1982) are used for small and medium-sized tumours of the skin, nose, lip and penis. The nickel needles are straight, bevelled and measure 20–80 mm in length, with an external diameter of 0 8 mm and internal diameter of 0.5 mm Individual pre-perforated plastic templates hold the needles in position.

Ninety per cent of patients with carcinoma of the lip presenting to the IGR are treated by interstitial methods with 90% local control and good functional and cosmetic results A review of 37 patients with carcinoma of the penis treated by interstitial curietherapy at the IGR shows a five-year survival of 81.2%, 12% have developed local recurrence and 15% required amputation for recurrence or complications. The majority have retained good function and cosmesis

Silk sutures are used for superficial skin tumours of the eyelid and ala nasae. The silk sutures are prepared in advance, each containing a length of lead wire, varied as required. Depending on tumour volume, appropriate lengths of iridium are substituted for the lead and the suture used to draw the source into place

Ninety-nine patients have been treated to a tumour dose of 69 Gy by this method, excellent results have been obtained, with two recurrences and cataract development in three.

Guide needles in templates (Papillon et al, 1973a,b) are an array of rigid hollow needles attached to a plastic template which holds the sources in the desired distribution. This technique is used mainly in the conservative treatment of carcinoma of the anus.

### *Conclusion*

The techniques of interstitial curietherapy at the IGR can produce excellent local control and survival in selected tumours with the added advantage of good patient tolerance, few sequelae and short treatment times Such techniques can be learned only by individual apprenticeship. At the IGR, curietherapy theatre sessions are held each morning, treating a wide range of tumours. During my stay, I observed all the above techniques, learned the principles of dosimetry and how these methods could be adapted to a variety of situations In a relatively short time, I saw more interstitial work than an average trainee in the United Kingdom might meet throughout the whole of training In addition, there were less easily quantifiable benefits of working in association with a team of different nationality, background, training and philosophy, those high standards of practice are to be admired

### *Acknowledgments*

This proved an excellent opportunity to broaden the scope of my training and I am grateful to the Northern Regional Health Authority which granted support and study leave, the BIR for sponsorship and the staff of the IGR. Special thanks are due to Professor Daniel Chassagne, Chief of Service, and Dr Alain Gerbaulet, Head of Department, for their teaching, encouragement and hospitality.

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# PACS meeting well attended

The BIR Industry Committee sponsored a meeting, held at the Middlesex Hospital Medical School on February 25, on picture archiving and communications systems (PACS), their practical uses and applications To the delight of the organisers, this meeting was attended by over 230 participants, representing industry, radiology, and radiography

The meeting was opened by the President, Professor Roger Berry, and chaired by Professor Ian Isherwood. Professor Isherwood outlined the size of the medical market for PACS systems, and reminded the audience that although the application of technology to the clinical environment could be stimulating and rewarding, we should all bear in mind the goal of improving the well-being of the patient.

Dr Craig, of St Mary's Hospital, Paddington, gave a realistic insight into the problems of establishing a digital diagnostic department, enthusiasm and commitment shone through a saga of success, failure, hope, and practical reality It was obvious from the experiences of Dr Craig that a truly digital department is still many years away, although steps in that direction can be made and implemented now. After coffee, the next speaker was Mr David Rothery of 3M, who gave the audience a clear and informative resumé of the technology and assorted resolutions required for different clinical images Dr Chris Taylor followed with an in-depth look at pattern recognition, and image interpretation and "interrogation". Dr Bill Lees expounded the radiologist's requirements and gave those members of the audience from industry considerable food for thought. as he said, 16 megabytes of information in a chest radiograph can be reduced by a radiologist to the word "normal" Mr Brian Dalton, the final speaker of the morning session, discussed image analysis, comparing the eye with video displays At the end of his presentation an impressive video was shown of a section through the heart, demonstrating real-time blood flow, with deoxygenated blood represented in blue and oxygenated blood in red

After lunch, Dr Rupprecht of Kodak presented information obtained from surveys in the USA, which reiterated the points made by Dr Lees systems will not be accepted if they are expensive and produce only poor information Mr Hugh Griffith, a neurosurgeon from Bristol, described how the transmission of computed tomography images around Bristol was improving the management and speed of treatment He made several controversial statements, stimulating the audience, and pointed out that a very cheap way of storing clinical images was to give them to the patients, as is the practice in other European countries Professor Gillanders, from Aberdeen, described long-distance telemedicine Mr Philip Vernon, of IGE, described the results of a joint research project to develop a clinically useful PACS system with IBM and Kodak While these results were technically very impressive, I was left with the impression that current systems fall short of the requirements proposed by Dr Lees. Colin Robertson of the DHSS, Mr Tiemann of Philips, and Dr Greinacher from Siemens all discussed PACS systems from their own point of view

The meeting concluded with a panel discussion, lead by Professor Isherwood I was left with the impression that, based upon the broad-ranging discussions during this very worthwhile day, PACS still has a long way to go before full clinical acceptability is achieved

John Twydle

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# Radiology '87: conference report

The following is a report by F John L Bindon, Press Officer for the Institution of Nuclear Engineers, who was a guest at Radiology '87 and here gives an "outsider's" view. The official BIR report of the Congress will be featured in next month's *Bulletin.*

In the excellent setting of Southampton University's purpose-built conference centre, the BIR staged Radiology '87, its 45th Annual Congress in this, its 90th year

As an invited press visitor to the Congress I was very impressed with the organisation of the whole event. not just the scientific and technical papers presented, but the accompanying exhibition and the care taken to ensure that all delegates had a very enjoyable social time throughout the three days

Some 470 radiologists, radiographers, scientists and engineers from home and abroad participated in a wide-ranging programme of some 200 papers in oral and poster sessions. To select, referee and arrange such a programme and do so successfully warrants special congratulations to the Scientific Programme Committee under its Chairman, Dr Peter Smith

My particular interest in the conference was brought about because of the decision made by the BIR to stage an all-day general-interest seminar on the medical consequences of reactor accidents This seminar attracted a great deal of popular interest, centring upon the Chernobyl accident The fact that two speakers from the USSR gave an account of their clinical experience following the catastrophe at Chernobyl certainly enlivened delegates Among the range of presentations made, one must speak highly of the first paper, by Dr Lushbaugh from Oak Ridge, Tennessee He described how the carefully annotated studies of 284 radiation accidents shaped the medical care afforded to more than 200 severely irradiated victims at Chernobyl Of the other invited presentations at this seminar, Dr Roger Clarke, Director designate of the National Radiological Protection Board (NRPB), made some interesting comparisons of the significant releases to the environment and exposures to the public from three major accidents, Windscale, Three Mile Island and Chernobyl. He outlined the cause of each accident and explained why the composition of the released radionuclides differed.

The Congress presented three very prestigious lectures The Mayneord Lecture followed the day-long seminar on nuclear accidents and their management. This lecture, sponsored by 3M UK PLC, was given by Miss Frances Fry of the NRPB, who presented a thesis in tune with the seminar of the day, entitled "Chernobyl reactor accident. the impact on the United Kingdom". She described the arrangements undertaken for environmental monitoring and the sequence of events in the early days following the accident, and examined all the measurements made on people and foodstuffs and the way all results were co-ordinated. It was a very well structured lecture, and was exceptionally well received.

The Congress organisers staged an excellent exhibition, described by the President as the "shop window" for the British radiological industry. It did show a most representative cross-section of all that is new in radiodiagnostic and radiotherapeutic equipment.

The social side of this Congress was no less enjoyable, made so by the many delegates engaging themselves with friends and the making of new friends so as to express the greatest of courtesy and hospitality to newcomers and non-members alike This stemmed from the help of the organising team and the very energetic effort made by the President, Professor Berry. In no small way was the success of this Conference due to him

For all those members of the BIR who have, perhaps, never attended such an event, I would suggest an early booking for 1988 when the venue is Glasgow

F JOHN L BINDON

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# International Conference on the Biological Effects of Ionising Radiation

Hammersmith Hospital, November 24–25, 1986

*The following conference report was provided by Dr Robin Russell Jones. Dr Jones is Chairman of Friends of the Earth Pollution Advisory Committee and was the conference organiser. The views expressed in the report and interpretations drawn from the meeting are those of Dr Jones and do not reflect in any way the opinion of the British Institute of Radiology or the Journal—Editors.*

The decision by Friends of the Earth to organise an international conference on the biological effects of ionising radiation stemmed from the recognition that the nuclear debate was increasingly polarised and in danger of becoming incoherent Two areas in particular seemed to require urgent reappraisal the estimates of cancer risk per unit dose from the International Commission on Radiological Protection (ICRP), and the epidemiological data on leukaemia clustering in the UK. Important new data on both these issues had been presented at the Dounreay public inquiry into the proposal by the UK Atomic Energy Authority to build a new European reprocessing plant, and Friends of the Earth felt that these data should be debated in a public arena The Chairman of the National Radiological Protection Board, Professor Sir Richard Southwood, F R S, agreed to chair the conference, which was held at the Royal Postgraduate Medical School.

The ICRP risk estimates were debated on Day One of the conference. Professor Edward Radford presented an updated analysis of the data from the atomic bombings indicating a cancer risk per rad in the survivors four times higher than that offered in ICRP Report 26. Dr Valerie Beral from the London School of Hygiene and Tropical Medicine presented her mortality data on the UK nuclear workforce which, despite the wide confidence limits, also indicated that ICRP underestimates the true leukaemia and cancer risk per rad

David Gee representing the General Municipal and Boilermakers Union argued for a reduction in occupational dose limits by a factor of five, to one rem per annum, and Professor Karl Morgan a former member of the ICRP main committee, claimed there had been a failure to warn of the dangers of uranium mining, mass radiological screening and weapons fallout Professor Roger Berry, a serving member of the ICRP, explained that the dose limits are not limits which can be regarded as safe: rather, they are limits which mark the boundary of unacceptability He emphasised that in practice actual exposures are well below the dose limits laid down by ICRP because of the ALARA principle keeping all doses "as low as reasonably achievable". In the discussion which followed this approach was challenged Several speakers emphasised the difficulty of applying ALARA in practice, and argued that the only certain method of reducing occupational exposure was to lower the maximum permissible limit. Other speakers questioned whether ICRP is an appropriate organisation be taking decisions about what is acceptable and unacceptable to workers and to the public David Gee criticised the fact that the ICRP does not include any representative of any organisation whose members actually carry the risk of what is deemed acceptable by ICRP.

A major criticism concerned the ICRP weighting factors, which convert organ doses to whole-body equivalents, since these factors have resulted in an increase in the permissible doses to individual organs. Thus ICRP Report 26 which was published in 1977 allows a gonad dosage to workers of 20 rem per annum, four times the previous limit. The permitted dosage to bone marrow has been increased by a factor of 8 and to tissue such as lung, thyroid and breast by factors of 1.5 to 3. To many in the audience it was difficult to reconcile these increases with the concept of ALARA If these organ dose limits were reasonably achievable in 1957 why were they not achievable in 1977, particularly as the dangers of ionising radiation are better understood than previously? Professor Berry did not attempt to defend these increases but indicated that both the cancer risk per rad and the weighting factors would be reviewed at the forthcoming ICRP meeting in Como this year

Achieving a consensus on the issue of leukaemia clustering proved more difficult. The relevant session on Day Two was chaired by Sir Douglas Black, who produced the report on the excess cases of leukaemia around Sellafield two years ago Since then another highly significant leukaemia cluster in children has been identified around Dounreay, the only other reprocessing facility in the UK Furthermore, data collected by the Scottish Health Agency had identified excess cases of leukaemia around three other nuclear facilities in Scotland Rosyth, Hunterston and Chapel Cross. A survey of leukaemia throughout the whole of Scotland had shown that the distribution of childhood leukaemia conformed to a Poisson distribution with no evidence of clustering in areas away from nuclear facilities At the conference John Urquhart, who originally helped to identify the Sellafield cluster, presented mortality data on 14 other nuclear facilities in England and Wales and showed that within a 12.5 km radius there was a modest but significant excess of leukaemia deaths in rural but not in urban children from 1965 to 1980. In the face of these new data in seemed apparent that Sir Douglas Black would need to modify the position which he adopted two years previously. While it might be possible to dismiss one cluster on the basis of chance, it could be difficult to ascribe all these events to random variation. On Sellafield Sir Douglas conceded that the undisclosed discharges which had come to light since his inquiry reported made him less happy about the qualified reassurance he had offered local residents. But on the new epidemiological data he ventured no opinion

There were several other papers which presented important new data on the low-level radiation controversy. Sarah Darby and Richard Doll looked at leukaemia incidence in Norway, Denmark and the UK to see whether the childhood rate was influenced by the atomic weapons fallout This peaked in 1962 but was followed by a rise in leukaemia incidence only in the UK, an anomaly which requires some explanation Dr Alice Stewart presented a paper showing that the background level of ionising radiation influences mortality from childhood cancer in the UK. This analysis used two data sources the Oxford Survey of Childhood Cancers (which now contains $347 \times 10^6$ person-years of follow-up) and the National Radiological Protection Board's Survey of Background Radiation Levels Throughout the British Isles Alice Stewart's data indicated that the cancer-doubling dose for *in-utero* exposure to the $\gamma$-ray component of background radiation is about 160 mrem per annum. This contrasts with the allowable public exposure limit around nuclear facilities in the UK of 500 mrem in any one year Recently both ICRP and NRPB have recommended a lower limit of 100 mrem per annum for lifetime exposure, but Dr Stewart's analysis suggests that even this may be too high

On the other hand, it has to be recognised that Alice Stewart's positive findings are in conflict with Sarah Darby's negative findings Doses for weapons fallout were equivalent to background radiation, so why was no increase observed in countries such as Norway and Denmark following weapons fallout in the '60s? One explanation might be the different methods of analysis. Alice Stewart divided her population into birth cohorts whereas Darby looked at new cases per annum If Alice Stewart's thesis is correct that childhood cancers are induced *in utero*, then analysis of birth cohorts should prove a more robust and sensitive technique than crude incidence data

Only a complete optimist would expect all of these issues to be satisfactorily resolved during the course of the conference. Nevertheless, the conference was unique in bringing together the main protagonists in the low-level radiation controversy Certainly a better awareness of the other side's point of view will flow from this event The proceedings will be available later this year, edited by Professor Sir Richard Southwood and Dr Robin Russell Jones, and published by John Wiley under the title *Radiation and Health, the Biological Effects of Low Level Exposures to Ionising Radiation*

ROBIN RUSSELL JONES

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# Stanley Melville Memorial Award 1987

The Stanley Melville Memorial Award for 1987 has been awarded to Dr R G. Henderson, Senior Registrar at Brompton Hospital, London The Institute will contribute to Dr Henderson's visit to the Christian Medical College, Ludhiana, Punjab, and the Indian Radiological and Imaging Association, New Delhi. During his stay he plans to combine some teaching with a study of the relevance of new imaging techniques in a developing country

This triennial BIR award was established in 1948 to enable members to visit clinics and institutions abroad.

## Aberdeen scientist honoured

An important honour and award has been made to Professor John Mallard of the Department of Bio-Medical Physics and Bio-Engineering of the University of Aberdeen and Grampian Health Board It is the 1987 Award of the European Workshop of Magnetic Resonance in Medicine. It was presented at a dinner during a conference held by the European Society of Magnetic Resonance in Medicine and Biology, of which Professor Mallard was the Founder President, and the European Federation of Medical Physics Professor Mallard said that he accepted it on behalf of a very hard-working team of scientists, engineers and clinicians in Aberdeen He expressed his pleasure that the award was being made at a conference in which three institutions devoted to the European ideal were participating

# Press releases

**Philips and GEC to co-operate in medical systems**

Philips and GEC intend to concentrate the whole of their medical systems activities into a new, jointly owned company in which they will participate equally The joint company, which will combine the activities of Philips Medical Systems Division and GEC's subsidiary, Picker International, will have its headquarters in the United States The management will be headed by a Chief Executive Officer to be appointed by agreement between the parties upon nomination by Philips

GEC's medical systems activities are organised in Picker International, Inc., a US corporation with its headquarters in Cleveland, Ohio. Manufacturing and distribution facilities are in the US (where 4000 of its 6000 people are employed), Canada, the United Kingdom, West Germany, the Caribbean and Japan. Picker International's sales in the year ended March 31, 1986, were $612 million Philips Medical Systems Division, which employs 11 000 people world-wide (8500 in Europe), is based in Best, the Netherlands, with manufacturing facilities in the US, West Germany, the Netherlands, France, Italy and the United Kingdom Sales in the year to December 31, 1986 were Dfl.2824 million.

Both companies believe that combining the strengths of Philips Medical Systems and Picker will enable the joint company to meet the ever-increasing demands on resources for research, development and investment, because of rapid medical and technological innovation, and the need to remain competitive on the world market

**Change of address for Wolverson . . .**

Readers may find it useful to note that Wolverson X-Ray & Electro Medical Limited has moved its London office to the following address

Troy House Chambers
Elmgrove Road
Harrow
Middlesex HA1 2QQ

The telephone number remains unchanged at 01-427 2630.

**. . . and for Cea (UK)**

Will readers please note that (as of March 2 this year) the address for all orders and enquiries for Cea Medical X-ray Products is now

Nissen House
Grovebury Road
Leighton Buzzard
Bedfordshire LU7 8SS
(Tel 0525-382529)

# BIR calendar events

*Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).*

*The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.*

**Imaging in Dementia**
October 15, 1987 at 5.30 p m.
Organised by the Diagnostic Methods Committee. Speakers Prof. R Levy, Dr R Wise, Dr P J Ell, Dr N Artoun and one other.

**Chemical Modification of Radiation Effects: Experimental and Clinical**
November 13, 1987
All-day radiobiology work-in-progress meeting

**New Radiopharmaceuticals and Their Clinical Applications**
November 27, 1987
Scientific Societies, London W1
Organised by the Nuclear Medicine Subcommittee
Speakers. Dr I Brown, Dr B. Langstrom, Prof N. A Lassen, Dr H J Machulla, Dr A. D. Nunn, Dr J. Thornback and Dr G. D. Zanelli

**Joint BIR/RCR/RSM Meeting**
January 14, 1988 at 5.30 p m

**Clinical Usefulness of Nuclear Medicine Image Data Processing**
February 10, 1988
Joint IPSM/BIR meeting organised by the IPSM.
Further details· General Secretary, IPSM, 47 Belgrave Square, London SW1 (Tel 01-235 6111).

**Institute Sponsored Visits**

Members should write to the General Secretary of the BIR for application to either of the visits below

**Stockholm:** to the clinic of the late Dr Curt Westman, now owned by AB Medicinsk Roentgen

**Paris:** to radiotherapy centres in Paris, arranged through the collaboration of Professor M. Tubiana

**British Institute of Radiology 46th Annual Congress**
*incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting and in collaboration with the Scottish Radiological Society*

## Radiology '88

Glasgow May 23–25, 1988

Glasgow will be the first in a series of back-to-back meetings with the Annual Conference of the College of Radiographers. The technical exhibition will span both meetings and be the manufacturers' showcase in 1988

The place the brand new Scottish Exhibition and Conference Centre.

Radiology '88 will cover all aspects of radiology X-ray diagnosis, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines

Proffered papers and posters are invited: closing date November 30 1987

**Functional Insights Using Magnetic Resonance Imaging**
February 17, 1988
London, venue to be confirmed
Organised by the Diagnostic Methods Committee.

**Radiobiology All-Day Non-topic Proffered Papers Meeting**
February 19, 1988
Organised by the Radiobiology Subcommittee.

**New Demands on Diagnostic Equipment to Reduce Radiation Dose**
March 9, 1988
All-day meeting organised by the Industry and Radiation Protection Committees

**Total-Body Irradiation**
April 13, 1988
Joint BIR/IPSM meeting organised by the BIR.

**Conversazione**
June 23, 1988
Institute of Directors, London SW1

# Library news

**The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)**

*The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a m–5 p.m., and Thursdays 11 a.m.–7 p m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel 01-580 4085).*

*The journal stock includes more than 100 titles Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the* Bulletin *Most books (excepting the historical collection) are available on loan*

*There is an agreement which allows BIR members limited use of the RSM Library for reference purposes Members should apply to the BIR Librarian for a visitor's card.*

**Recent additions to the Library**
Carruth, J A. S. & McKenzie, A L Medical lasers. Science and clinical practice. 1986
Haywood, J. K (Ed ) Chernobyl: response of medical physics departments in the UK (IPSM Report No 50) 1986
Levy, R. C, Hawkins, H & Barsan, W. G.· Radiology in emergency medicine. 1986
Maklad, N F (Ed )· Ultrasound in perinatology (Clinics in diagnostic ultrasound. 19). 1986
O'Reilly, P H., Shields. R. A. & Testa, H J Nuclear medicine in urology and nephrology. 1986

New Periodical:
IAEA newsbriefs

**Volumes of *BJR* for a good home**

A complete set of *BJR* (unbound) 1962–85 is available for donation. Please contact the Editorial Office (01-580 4189) to arrange for collection

**BIR Ties**

BIR ties are available to members at £5 each (£6 including post and packing). They are navy-blue or maroon red and carry the rays from the Institute's logo, in gold Please send a cheque payable to the BIR with the order.

# Meetings and courses

*As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge any additional information will be charged at £1 75 per printed line, per insertion Please contact the Managing Editor*

**Chest Imaging Conference (CIC-87)**
August 31–September 2, 1987
Madison, Wisconsin, USA
Further details John R Cameron, Department of Medical Physics, 1530 MSC, 1300 University Avenue, Madison, WI 53706, USA (Tel 608-262 2171).

**International Symposium on Dosimetry in Radiotherapy**
August 31–September 4, 1987
Vienna, Austria
Further details Secretariat IAEA-SM-298, c/o International Atomic Energy Agency, PO Box 100, A-1400 Vienna, Austria (Telex No. 1-12645 Cable address INATOM VIENNA)

**The Bart's MCQ Course (FRCR II)**
September 1, 1987
St Bartholomew's Hospital, London
Further details Mrs C Burrage, MCQ Course Secretary, Room 26 Dunn Laboratories, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE (Tel 01-601 7531)

**Symposium Mammographicum**
September 3–4, 1987
Nottingham
Further details· The Conference Officer, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG (Tel 01-636 4432/3)

**Current Dilemmas in Gynaecological Oncology**
September 3–5, 1987
University of Birmingham
Further details: Conference Organiser (ONC), Bell Howe Conferences, Gothic House, Barker Gate, Nottingham NG1 1JU (Tel. 0602-410 679)

**St Bart's Megavoltage Radiotherapy 50th Anniversary Conference**
September 3–5, 1987
St Bartholomew's Hospital, London
Further details The Secretariat, Concorde Services, 10 Wendell Road, London W12 9RT

**1st Copenhagen Symposium on Uroradiology: Imaging and interventional techniques**
September 7–10, 1987
Herlev Hospital, University of Copenhagen, Denmark
Further details Dr Henrik S Thomsen, Department of Diagnostic Radiology 54E2, KAS Herlev, Herlev Ringvej, DK-2730 Herlev, Denmark

**XIVth Congress of the European Society of Neuroradiology**
September 8–12, 1987
Udine, Italy
Further details M. Leonardi, Servizio di Neuroradiologia, Ospedale Civile, 33100 Udine, Italy

**HPA Annual General Meeting and IPSM Scientific Meeting**
September 15–19, 1987
Liverpool
Further details IPSM, 47 Belgrave Square, London SW1X 8QX (Tel. 01-235 6111)

**3rd Annual Clinical Hyperthermia Symposium and Workshop**
September 17–19, 1987
St Louis, Missouri, USA
Further details. Bahman Emami, M D., Symposium Chairman, Division of Radiation Oncology, Mallinckrodt Institute of Radiology, 4939 Audubon Avenue, Suite 5500, St Louis, Missouri 63110, USA (Tel. 314-362 8500)

**5th Asian-Oceanian Congress of Radiology**
September 21–25, 1987
Seoul, Korea
Further details. Man Chung Han, M D., Secretary General, 5th Asian-Oceanian Congress of Radiology, c/o Department of Diagnostic Radiology, Seoul National University Hospital, 28 Yunkun-dong, Chongro-ku, K.P.O. Box 1880, Seoul 110, Korea

**6th International Workshop on Bone and Soft Tissue Densitometry**
September 22–25, 1987
Palace Hotel, Buxton, Derbyshire
Further details Dr J. E Adams, Senior Lecturer, Department of Diagnostic Radiology, Stopford Building, Oxford Road, Manchester M13 9PT

**International School on Monte Carlo Transport of Electrons and Photons Below 50 MeV**
September 24–October 3, 1987
Erice, Sicily
Further details A E Nahum, Physics Department, Royal Marsden Hospital, Sutton, Surrey SM2 5PT (Tel 01-642 6011)

**5th International Congress on the Ultrasonic Examination of the Breast**
October 3–5, 1987
New Orleans, Louisiana
Further details Department of Radiological Sciences, University of California Medical Center, Irvine, University Hospital, 101 City Drive South, Orange, California 92668, USA

**Radiology and Management of Trauma Course**
12–15 October, 1987
Leicester Royal Infirmary
Further details· Dr D Finlay, Consultant Radiologist, Leicester Royal Infirmary, Leicester LE1 5WW

**8th Annual Study Day: the Role of the Plain Abdominal X-ray in the Acute Abdomen**
October 13, 1987
Canterbury
Further details. Dr Stuart Field, Consultant Radiologist, Kent and Canterbury Hospital, Canterbury CT1 3NG

**BMUS 19th Annual Scientific Meeting**
December 8–10, 1987
Brighton
Further details Dr R J Burwood, Department of Radiology, Royal Sussex County Hospital, Brighton, Sussex BN2 5BE

**International Congress: Interventional Radiology in Cardiovascular Diseases**
February 3–5, 1988
Toulouse, France
Further details Professor F Joffre, Service de Radiologie, Chu Rangueil, Chemin du Vallon, 31054 Toulouse Cedex, France (Tel. 6155 4478 ext 3081–3047)

**4th Jahrestagung der Deutschen Gesellschaft für Lasermedizin**
October 5–8, 1988
Vienna, Austria
Further details Doz Dr A Tuchmann, c/o Wiener Medizinische Akademie, Alser Strasse 4, A-1090 Vienna, Austria (Tel 0222-427 165)

**Workshop: Progress in Regional Cancer Therapy**
November 3–5, 1988
Vienna, Austria
Further details c/o B Schick, Abteilung fur Experimentelle,· Chirurgie der I Chirurgischen Universitatsklinik, Alser Strasse 4, A-1090 Vienna, Austria (Tel 0222-4800/2301)

# Ninth
# London Ultrasound Course

November 9–13th 1987
Skyway Hotel, Hayes, Middx.

This course in clinical ultrasound is designed to cover non-obstetric abdominal scanning in depth, but will also cover some non-abdominal applications

The course will consist of a combination of lectures, tutorials and supervised practical scanning tuition on state of the art scanners.

The course will be limited to 60 participants

*Course leaders:* David Cosgrove, Keith Dewbury, Hylton Meire.

*Further information from:*

Dr. H. B. Meire, X-Ray Department,
King's College Hospital,
Denmark Hill, London SE5 9RS.

To appear in *The British Journal of Radiology*

**Nuclear Reactor Accidents: Preparedness and Medical Consequences**
Full proceedings of a one day seminar held at the BIR annual congress in April 1987. Chaired by Sir Donald Acheson, this timely seminar brought together eminent speakers from the UK and abroad. Papers include:

- **Medical/radiobiological basis of radiation accident management** Dr C C Lushbaugh (USA)
- **Medical basis for the establishment of intervention levels** Dr J C Nénot (France)
- **Clinical experience of reactor accident management** Drs E Komarov and N M Nadezhina (USSR)
- **The role of NHS hospitals in the preparedness for nuclear reactor accidents** Dr P Bourdillon (DHSS, London)
- **Chernobyl reactor accident: the impact on the UK** Miss F A Fry, (NRPB Oxford) 1987 Mayneord Lecture

*To purchase extra copies of this special BJR issue, or reprints, please write to:*
**Publications Department**
**The British Institute of Radiology**
**36 Portland Place, London W1N 4AT**
**Tel: 01 580 4085**

8TH ANNUAL STUDY DAY

# THE ROLE OF THE PLAIN ABDOMINAL X-RAY IN THE ACUTE ABDOMEN

**TUESDAY 13 OCTOBER 1987**

**KENT POSTGRADUATE MEDICAL CENTRE AT CANTERBURY**

A comprehensive and critical analysis of the plain abdominal radiograph and its correlation with operative and postmortem findings.

Aimed at SHOs, Registrars and Senior Registrars in Surgery and Radiology, particularly those preparing for Fellowship examinations (the event has been approved for study leave).

Fee £30 including coffee, lunch and tea. Details from the Postgraduate Administrator, Kent Postgraduate Medical Centre, Kent & Canterbury Hospital, Canterbury, Kent CT1 3NG. Tel: (0227) 66877 ext. 4367.

## RADIOLOGIST CANADA

Radiologist wanted, with CT experience, to join small group of radiologists in regional referral center in small university city on east coast of Canada.

New "state of art" CT scanner being installed August, 1987.

Present services include nuclear medicine, angiography, ultrasound, mammography and special procedures

This position is long term, but applications for short term will be given very favourable consideration.

Send applications to:

Dr. J. A. Hardy
Secretary
Department of Radiology
Sydney City Hospital
Sydney, Nova Scotia B1P 2H8
CANADA

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**Royal Children's Hospital**

Flemington Rd., Parkville, Victoria,
3052, Australia.

## SENIOR REGISTRAR AND FELLOW IN PAEDIATRIC RADIOLOGY

Applications are invited for these positions for 12 months commencing February, 1988 at the Royal Children's Hospital, Flemington Road, Parkville, Victoria 3052, Australia

These positions would suit persons considering a career in Diagnostic Paediatric Radiology, or in their final year of training for the D R A C R

This Hospital is the principal paediatric tertiary referral centre for the state of Victoria and adjacent areas of neighbouring states The Hospital has 440 beds and is the paediatric teaching hospital for the University of Melbourne

The Department of Radiology is well equipped, and includes ultrasound, computed tomography and Nuclear Medicine Imaging Over 46,000 patient examinations are performed each year

Enquiries should be directed to Dr John De Campo, Acting Director of Radiology on (03) 346 5255 Applications should be requested from Mr Rod Griffith, Executive Assistant - Medical Administration, and forwarded to Dr Barry R Catchlove, Chief Executive by August 31st, 1987

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## RADIOLOGIST

**Required by large South African hospital practice based in Johannesburg.**
**Latest modalities include MR, CT and DVI.**

**Applicants for this post should be in possession of an F.F.R. degree (or equivalent).**

**Excellent salary and fringe benefits offered. Quality housing with pool and company car included. Relocation expenses will be paid.**

***Applications, together with detailed curriculum vitae should be addressed to:***

**The Business Manager,**
**P.O. Box 17473,**
**Hillbrow 2038, Transvaal,**
**South Africa.**

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## SENIOR MEDICAL PHYSICIST

Ph.D. level radiation physicist wanted to coordinate daily clinical radiotherapy physics, a large Brachytherapy Program with adjunctive interstitial hyperthermia, stereotactic radiosurgery and a teaching program for radiation therapy residents and technology students. Send current curriculum vitae to: Peter A. Fleming, MD, Head Division Radiation Oncology, **ALLEGHENY GENERAL HOSPITAL,** 320 E. North Avenue, Pittsburgh, PA 15212. An Equal Opportunity Employer.

AGH

*ALLEGHENY GENERAL HOSPITAL*

# The British Institute of Radiology Nycomed Scandinavian Scholarships 1988

The British Institute of Radiology invites applications for the 1988 Nycomed Scandinavian Scholarships.

These Scholarships, which are generously funded by Nycomed (UK) Ltd, enable United Kingdom diagnostic radiologists, preferably members of the British Institute of Radiology, to visit Scandinavian academic departments for up to two months' concentrated study, free of financial constraints: a maximum of £2500 per month will be provided.

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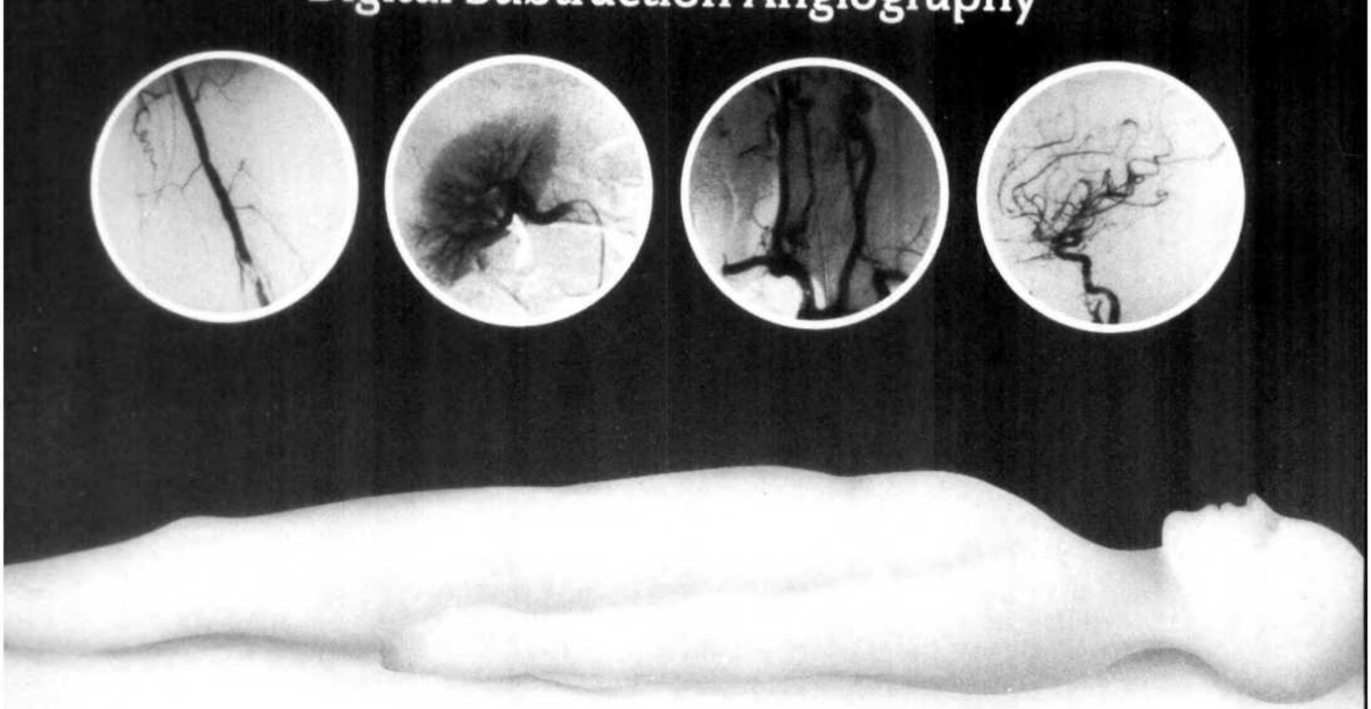

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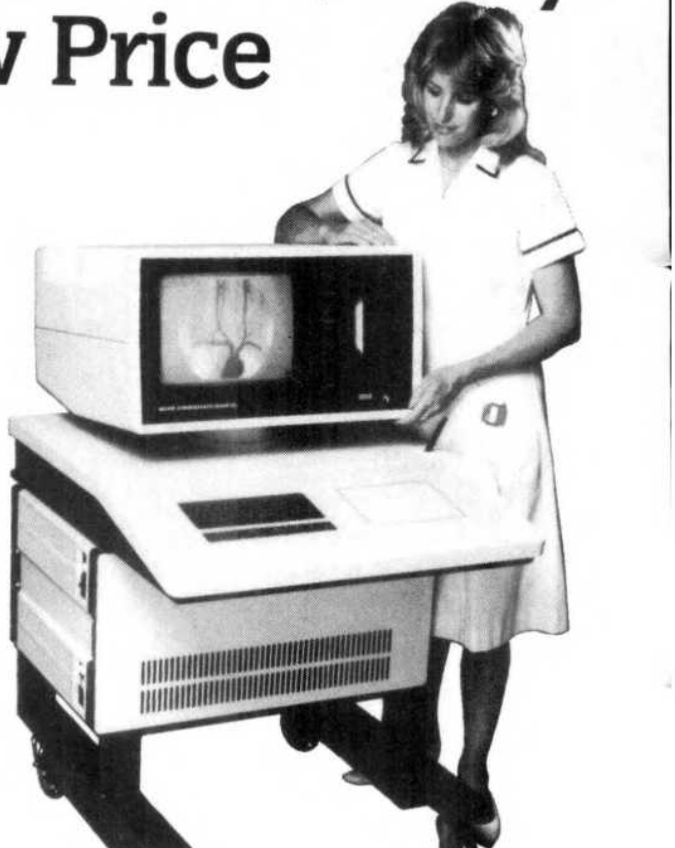

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Published by The British Institute of Radiology, 36 Portland Place, London W1N 4AT. Printed in Great Britain by The Whitefriars Press Ltd., Tonbridge. ISSN 0007 1285

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Volume 60 Number 716
August 1987

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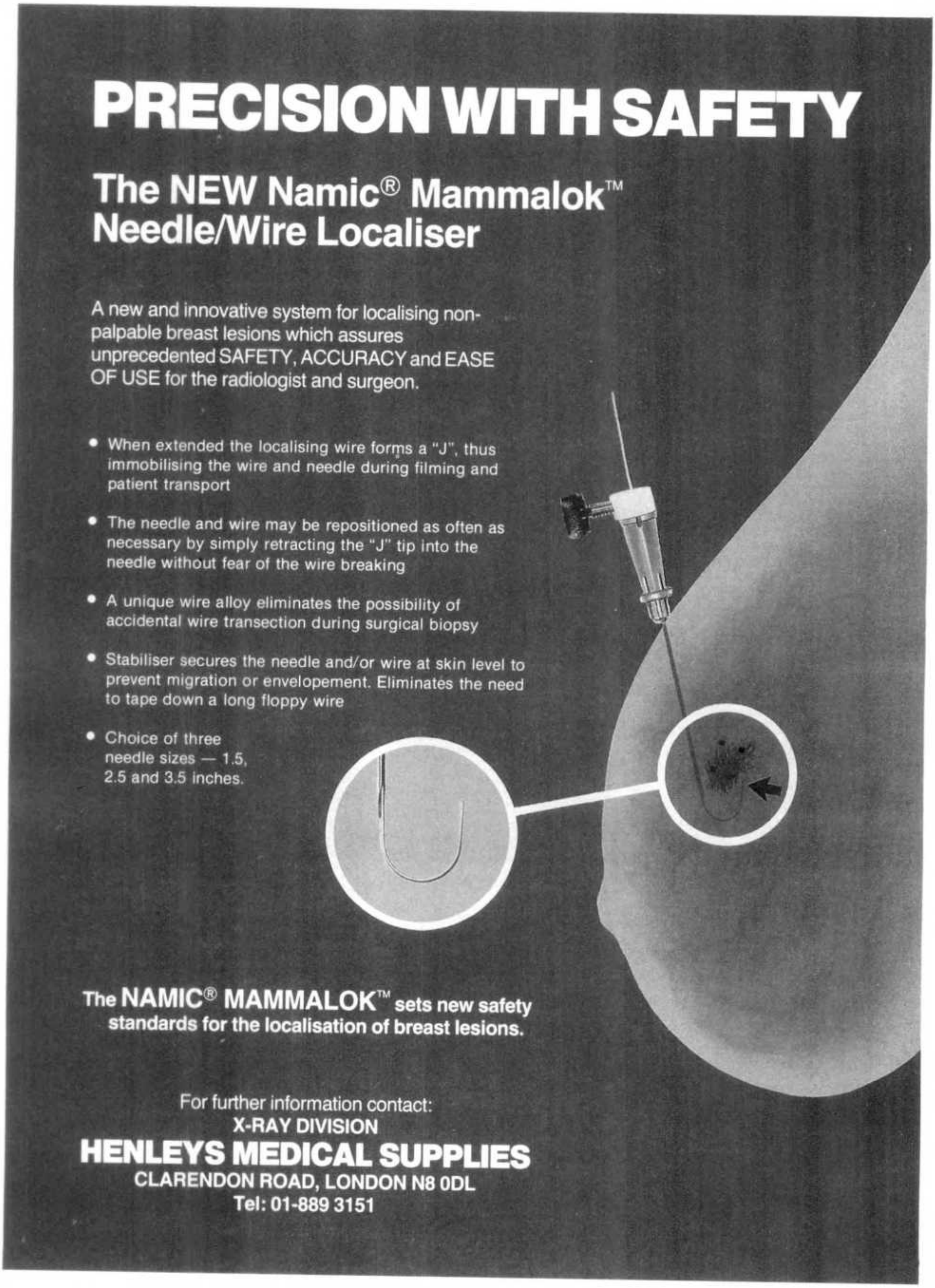

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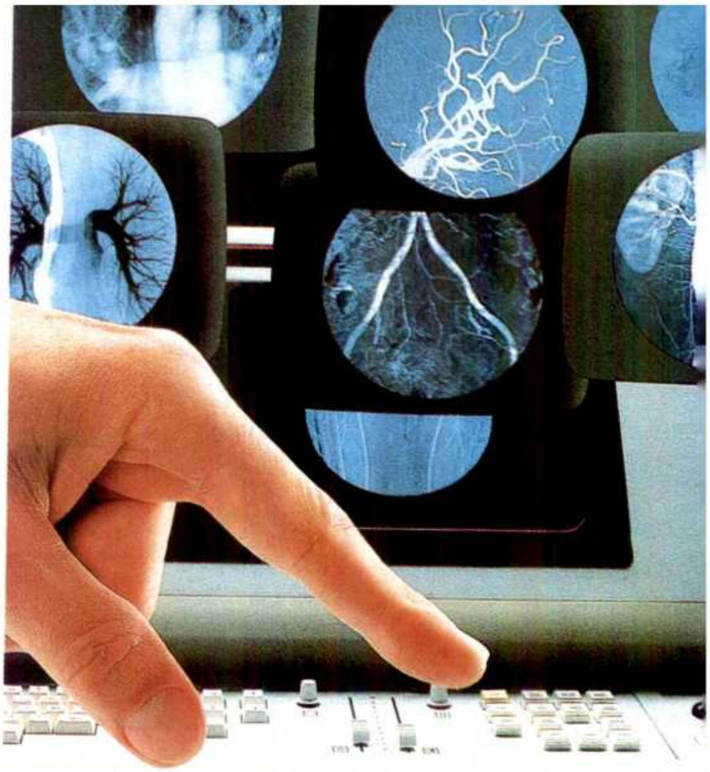

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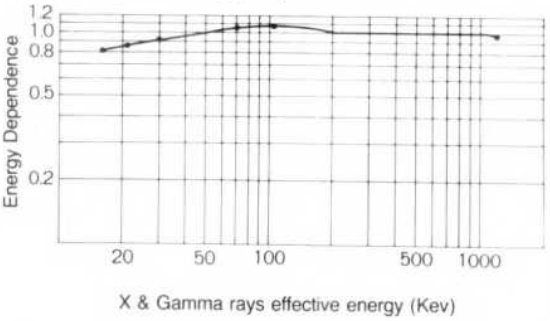

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British Journal of Radiology, Supplement 21

**Radionuclides in Brachytherapy: Radium and After**

Edited by N G Trott

This Report, prepared by a multidisciplinary working party set up by the BIR, reviews the clinical, dosimetric, radiobiological and practical aspects of brachytherapy using $\gamma$- and X-rays emitted by both natural and artificial radionuclides.

**Radionuclides in Brachytherapy** is a comprehensive introduction to the current state of the subject, as well as giving the background to the changes in techniques that have taken place during the last 40 years. Including tables, illustrations, a glossary and an outline of ICRU and BCRU recommendations plus a helpful list of manufacturers and suppliers, this report will be indispensable for anyone involved in theoretical or practical aspects of the radiotherapy, radiobiology or dosimetry involved in this method of treatment.

Publication date: late summer 1987

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1987, *The British Journal of Radiology*, 60, 735–751

VOLUME 60 NUMBER 716 AUGUST 1987

The British Journal of Radiology

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# Cancer: the failure of treatment*

By R. H. Thomlinson, M.A., M.B., B.Chir., F.R.C.R.

Breast Study Centre, Marie Curie Research Wing, Mount Vernon Hospital, Northwood, Middlesex

(*Received February 1987 and in revised form April 1987*)

Mr President, Ladies and Gentlemen. We all wish to improve the treatment of cancer and all must rejoice in success. It is both legitimate and necessary that we should turn our endeavours to alleviating or anticipating suffering and to prolonging life with at least a satisfactory quality, but in the last resort the measure of our success must be the cure of our patients.

## ANALYSE FAILURE, NOT SUCCESS

Biologically speaking, "cure" can only mean the total elimination of the population of neoplastic cells that have the quality of unlimited proliferation, that is to say, the clonogenic cells. Unfortunately there can be no absolute evidence that this complete elimination has been achieved. It is true that the statisticians can deal in terms of probabilities of cure which, in the case of some types of tumour, may give very high values, but the uncertainties involved do not provide a sure foundation for advance Patients today often receive several forms of treatment and in the event of success it is generally not possible to identify which aspect of the management decisively turned the scales or at what stage in the course of treatment this point was reached.

Failure, on the other hand, is all too definite. The timing of its occurrence may well be clear, the part of the body in which the treatment has failed may be obvious and the particular aspect of treatment at fault can often be identified. In short, "failure" is open to analysis in ways that cannot be applied to "success". As a generalisation I would urge that, in all investigations of new treatment, analysis of failure will result in a better way forward than concentration on success. I know that this is difficult for the medical mind and contrary to all our aspirations in becoming doctors, but the way of science is often hard.

## DATA FROM BREAST CANCER

In considering some of the biological factors that have led to failure I want to draw on our work over the last few years with carcinoma of the breast. Our hypotheses are based on the changes in volume of primary carcinoma of the human breast that accompany and follow treatment. We use the size of a tumour as a physical marker in a way analagous to that in which biochemical markers found in the bloodstream may be used in patients with certain types of tumour.

For this purpose it is first necessary to find a mathematical model that may be used to describe the accumulation of the crude data of the measurements in relatively simple terms. Such a model must be seen to form a good description of the best information, since any model may fit sloppy data.

All the statistics based on our observations have been calculated by a professional statistician. A detailed account of the methods and results is in preparation.

Within the range in which tumours in the breast may be measured in the clinic, both their growth and their resorption are well described by exponential regression lines (Figs 1, 2). Our data are based on more than 62 000 measurements of diameter made in 239 patients, giving 748 regression lines each averaging between seven and eight points (Table I). Five hundred and twenty-two of these lines represent the resorption of tumours and, of these, 70% have a $p$ value of less than 0.001, 12% not reaching the 95% level of statistical significance

There are fewer regression lines related to growth, namely, 226 The level of confidence in these is lower, partly because as soon as we were aware that a tumour might be growing we tried to stop it and partly, in the early stages of the investigations, because this growth occurred long after treatment and often when the patients were attending other clinics. We were not always made aware of this and so the measurements are fewer.

One of our observations has been of the relationship between the rates of resorption and growth. As is well known, tumours that go quickly tend to grow quickly. We have examined this relationship in 98 different primary carcinomas of the breast and although the coefficient of correlation is only 0.68, this is highly significant in a sample of this size ($p < 0.001$). It will need further analysis to establish an exact relationship between the two slopes. Because our data on resorption are more extensive and reliable than for growth, for certain purposes we have used the rate of resorption as indicative of the growth rate in tumours. Where this substitution is used it is stated.

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*The 1986 Silvanus Thompson Memorial Lecture, delivered in London on November 14, 1986.

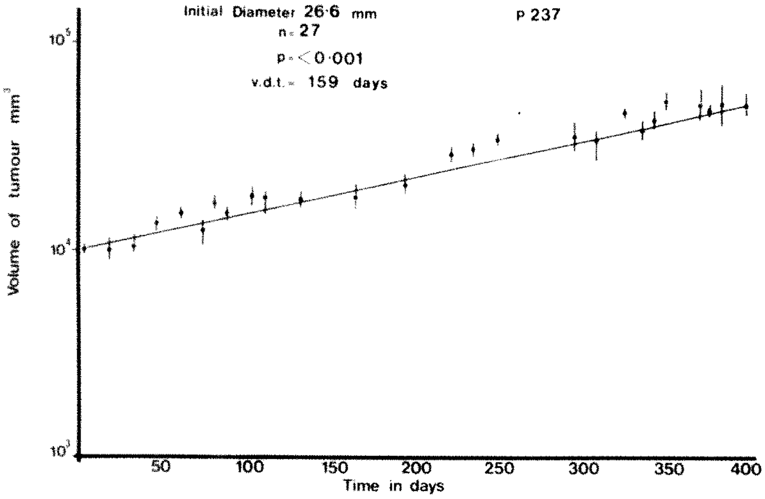

Fig. 1.

Exponential regression line fitting estimates of the volume of a tumour derived from caliper measurements of diameter during a period of growth. (v.d.t. = volume-doubling time). The data points are the means of the volumes calculated from each measurement of diameter and the error bars are the standard errors of the means.

### Clinical Trials and "Survival Time"

If the ultimate condition of success be cure, that of failure is the death of the patient. This, as an "end-point", is usually fairly definite, but the proportion of patients who die after this or that treatment is too crude a form of data to be of much analytical value in seeking the causes of failure. As an event, it is usually associated with the time at which it takes place, generally in the form of "survival time". But what are the factors that determine the length of this time? I should like to consider five as of paramount importance, though there may be many more.

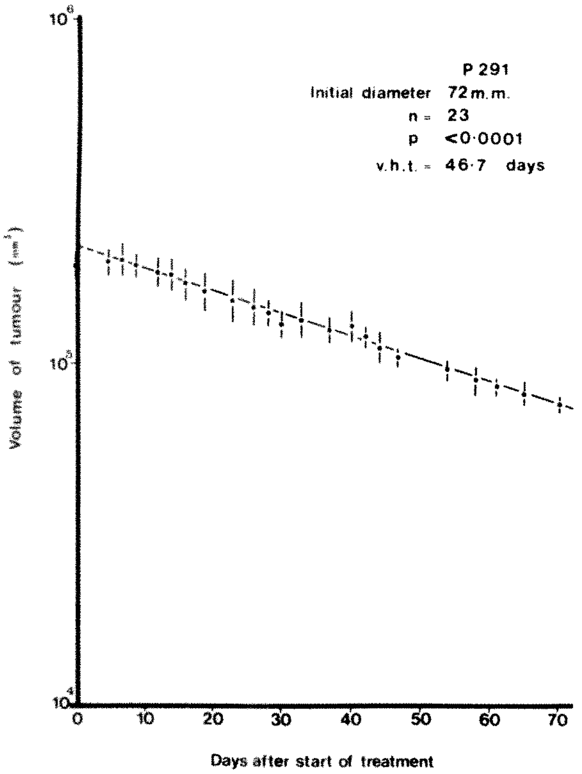

Fig. 2.

Exponential regression line fitting data for resorption of tumour after radiotherapy (v.h.t. = volume-halving time).

Firstly, the growth rate of the tumour. Were other things equal and no treatment given, the duration of the patient's life from the time of onset of the disease would be largely determined by this. In carcinoma of the breast our data suggest a range in excess of 50-fold. Though in other forms of tumour the rates of growth may be less varied they need to be determined and taken into account if the duration of survival is to be used as a measure of the effect of treatment.

Secondly, the stage that has been reached along the natural course of the disease when the period called "survival time" is initiated. The most important factor in this respect is probably the formation of metastases. This cannot be determined quantitatively, but the probability of its having happened increases with time and, were all else equal, the time in which it could have taken place is related to the size of the tumour. In our data concerning primary carcinoma of the breast, there is a range of volumes at the time of first treatment of over 1000-fold. For a tumour to increase in volume by a

TABLE I

Primary carcinoma of breast

| | | | | |
|---|---|---|---|---|
| Measurement of diameter | | | | |
| Total No. of observations | | | | 62 050 |
| Total No. of patients | | | | 239 |
| Total No. of regression lines | | | | 748 |
| Average No. of data points per line | | | | 7 |
| Regression lines | | | | |
| Significance level | >5% | <5% | <1% | <0.1% |
| Resorption slopes (522) | 12% | 88% | 82% | 70% |
| Growth slopes (226) | 24% | 76% | 66% | 46% |

factor of 1000 it must double its volume 10 times. Thus, this range of sizes involves a 10-fold range of growing times. The distribution of these sizes is another factor that needs to be quantified in relation to survival time. We have examined the relationship between the size of the tumour at the start of treatment and the rate of resorption, using this instead of growth rate, in 223 patients. The coefficient of correlation is 0.02: in other words, there is no evidence to show that there is a relationship between the two. It might be supposed that the propensity to form metastases is related to the growth rate of the tumour and that the likelihood that they have formed is related to its size. I find it salutary to remember that a patient coming with one of the largest tumours that we have seen (118 mm in diameter) and having a volume-doubling time of only 6 days, died more than 2 years later and that a search at post-mortem examination revealed no evidence of metastases. I think, therefore, that a factor at least of 10 must be allowed in the observed "survival time" because of differences in the stage of the disease when patients are first seen.

The third factor that I wish to consider in relation to the timing of death is the nature of the lesions that actually bring it about. Some say that it is the total quantity of tumour in the body that leads to death. I know of no evidence for this. Although I do not think that the total quantity has been estimated, every pathologist whom I have questioned agrees that it is very variable.

In general, neoplastic lesions produce their effects by interfering with the function of surrounding tissues. This is usually a mechanical effect of enlargement of the lesion causing interference with the blood supply and nutrition of nearby structures. Patients with multiple metastases in the liver die of a deficiency of functioning liver rather than an excess of neoplastic cells. Death depends on the particular vital organ where function is impaired. It can result from a solitary small metastasis in the mid-brain, whereas a patient may have a litre of tumour in the liver for some time before he dies as a result of liver failure. These extremes represent a range of more than 10 000-fold in the quantity of tumour that, in fact, has led to death. This range of quantity must be reflected in the time taken to cause this final event. Again, it would not be unreasonable to suggest a factor of 10 on the extent to which survival time could vary because of the site of the fatal lesions

The fourth condition that may affect survival time is the structure of the individual tumour. This is a topic to which I am going to turn in detail throughout the remainder of this lecture For the moment I want to suggest that differences in structure, at least in tumours of the breast, could add another factor of about 10 to the variation in duration of survival

Of course the fifth factor is treatment. One hopes that this may affect survival time. Obviously there are additional circumstances that may be involved but I think no scientist would seriously attempt to assess one variable, in this case the effect of treatment, from the combined effect of that and the other four variables that I have mentioned. Moreover, the magnitude of the first four variables is such that it would be quite impossible in practice to accumulate the numbers in a clinical trial that would balance them by a randomisation process. Survival time has an emotional value and we all hope that new treatments will lead to its prolongation, but its measurement is not a procedure that has the necessary resolving power for analysing the causes of failure in the treatment of cancer, at least in cancer of the breast.

The same arguments apply to some other systems that might be used for relating manifestations of the disease to time, for example, the duration of remission, or "symptom-free time".

## TUMOUR STRUCTURE AND SURVIVAL

I must now turn to the particular aspects of the structure of tumours that I have mentioned in relation to survival time and will introduce this by telling you about a single patient (Fig. 3). This lady presented with a tumour about 30 mm in diameter as measured in the clinic. She was treated by one of our colleagues with a standard form of fractionated radiotherapy and we were permitted to take measurements whenever she attended the department. At first the tumour became

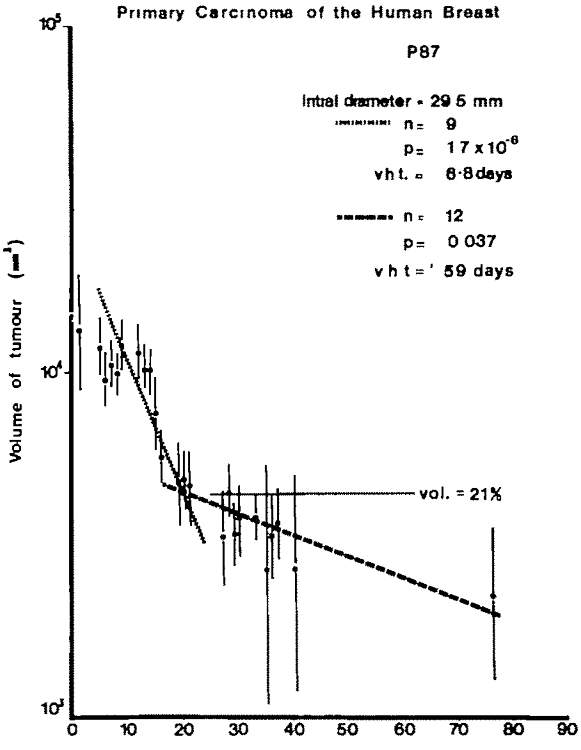

FIG 3

Biphasic regression line fitting data for resorption of a tumour with a central collagenous core following radiotherapy smaller quickly and then the rate of resorption changed The data on which the first regression line is based are good, for the second not so good because of the less frequent visits The change occurred when 21% by volume remained The first slope has a volume-halving time of 7 days, from which we would predict a volume-doubling time of 10–12 days.

We also have very nice histological material from a biopsy taken by a drill passing along the diameter of the tumour. In this the cell density is far greater at the periphery than in the central part and the converse is true of the collagen.

Measurements of the "tumour" *in vivo* and of the biopsy are consistent with the inclusion of two layers of skin and a little subcutaneous tissue as well as the actual tumour tissue in the former. Were 21% taken of the volume of a sphere calculated from the length of the biopsy it would correspond to a smaller sphere with a diameter of 10 mm. The change between the relatively cellular, peripheral part of the tumour and the centre is abrupt and the far less cellular part has a length in the biopsy of 10 mm. Thus there is agreement between measurement of the structure of the tumour and measurements of the way in which it responded to treatment.

The explanation of this change in composition rests on very extensive histological observation As a tumour grows the circulation in the central part becomes inadequate. When the growth rate of a tumour is high, the result is coagulative necrosis in the centre. Where the growth rate is lower, more collagen is likely to be formed as the tumour grows and death of cells when the circulation fails is piecemeal. Autolysis and resorption occur, leaving a condensation of collagen in the central part.

The centre of a larger tumour was once the peripheral part of a smaller one The failure of circulation leads to the death of most but not all cells and it is probable that those that remain are malnourished. They may therefore be protected from radiation injury by hypoxia and from poisoning by cytotoxic agents because the concentrations that reach them are sublethal

The tumour that I have just described grew again after 10 years. Radiotherapy failed to eliminate the neoplastic clonogenic cell population. But had cells survived in the well nourished peripheral part, even with the slowing of growth that occurs in an irradiated field, with a basic 10-day volume-doubling time, recurrence would have been evident within 2 years

The implication is that the renewed growth came from cells in the central portion. Not only may these have survived the radiation because of hypoxia, but, being malnourished, they may not have begun to proliferate again until the healing process brought a better blood supply The process, which pathologists call "organisation", must involve the removal of collagen. This occurs slowly, possibly with a volume-halving time as long as 5 months. Since it would take 29 halvings of volume to remove a sphere 10 mm in diameter, it is possible to account for the recurrence of apparent growth 10 years later by supposing that surviving cells came to be well nourished at some time fairly late in the intervening period and then started to proliferate again

If this explanation is correct, it may be seen how the structure of a particular tumour might play a large and fortuitous part in determining the duration of the patient's survival.

### Tumour Structure and Resorption

We can extend these ideas by comparing the response to radiotherapy and the structure of tumours in two particular patients who received rather similar treatment. The first of these tumours was 62 mm in diameter at the start of treatment and was resorbed to the point where only 6% by volume remained The 21 data points were well fitted by an exponential regression line ($p < 0\ 001$) giving a volume-halving time of 10 3 days. The tumour in the second patient had an initial diameter of 56 mm and the resorption down to 15% was also well fitted by an exponential regression ($n = 34$, $p < 0.001$) line but with a volume-halving time of 175.6 days

Resorption is the removal of the physical components of the tumour, samples of which may be studied in histological sections For these two tumours, again, we have good biopsy material. From the sections it can be seen that the central parts of the tumours contain higher densities of collagen than the periphery. It is therefore likely that the periphery is resorbed the more rapidly. In each I have therefore made measurements through the outer 11 mm of radius, resorption of which would account for the removal of 90% of each tumour. In this part the proportions occupied by parenchymal tumour cells and by collagen fibres have been estimated by visual morphometric methods (Chalkley, 1943) and plotted at 0.5 mm intervals from the edge of the tumour (Fig. 4).

In the more rapidly resorbed tumour, on average 60% of the outer part was occupied by parenchyma and 10% by collagen. There are other components, for example, oedema liquid, that would have been present in life but not visible down the microscope, parenchyma, therefore, was the major component that must have been resorbed in the removal of 90% of the mass Since oedema could go more quickly, it is likely that the parenchyma determined the actual rate of resorption and the collagen, being only 10%, played a very small role.

In the second tumour, by contrast, the parenchyma occupied only 12% of the peripheral part and collagen, 53% Thus, for the removal of 85% of the tumour volume much collagen would have been resorbed and it is the rate of this process that probably accounts for the volume-halving time of 176 days. These results have recently been confirmed by a surgeon colleague using sophisticated image analysis in a more extensive investigation (Moat, N., personal communication).

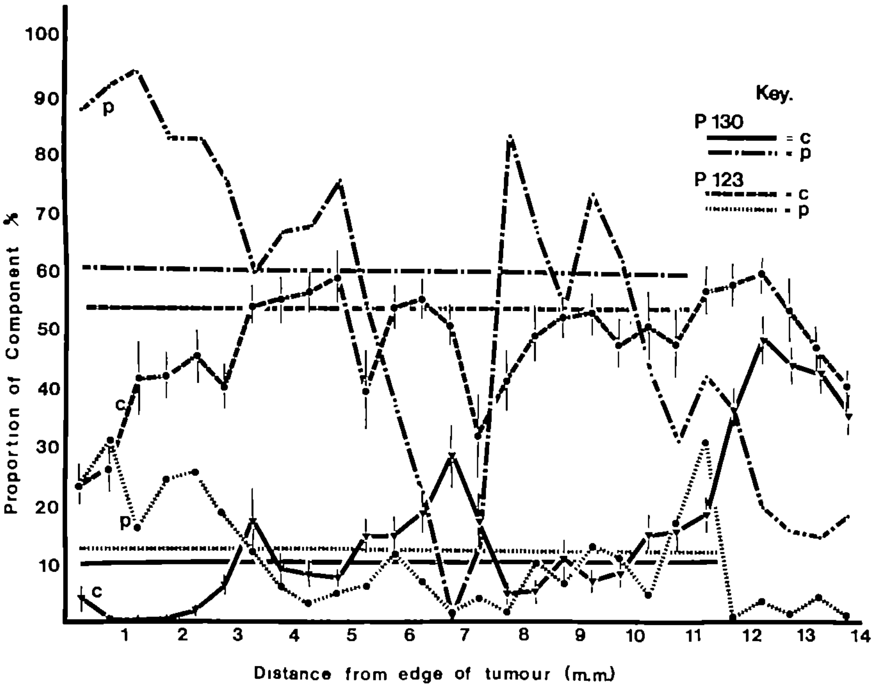

FIG 4

Proportions of collagen (c) and parenchyma (p) in relation to the distance from the edge of carcinomas of the breast in two patients (P130 and P123). The horizontal lines are the mean values of the components in the peripheral 11 mm of the radius of the tumours. This part of each tumour was resorbed after radiotherapy The volume-halving times for P130 and P123 were 10.3 days and 175.6 days respectively

I think that this type of investigation has an exciting future. It will help to clarify a confusion that has existed in clinical trials throughout the last 30 years, or rather will re-separate the fusion of two distinct problems that have bedevilled trials by their amalgamation. One question is that of the effects of different treatments on similar tumours and the other is that of the effects of the same treatment on dissimilar tumours.

The rate of resorption and its extent tell us something about the nature and composition of a tumour but not about the effectiveness of treatment.

From these investigations we are learning about the relationship between the composition and histological structure of the tumours and the type of biphasic curve that I have illustrated (Fig. 3). Composition changes with time as treatment proceeds. As was said of old by Heraclitus, the philosopher of continual change, "you can't step in the same river twice": so, you cannot treat the same tumour twice. All of these measurements are providing a guide to how we should change the management of individual tumours as time passes.

## RESORPTION AND CELL SURVIVAL

We must, however, take one more look at the relationship between the way in which tumours become smaller and the treatment that has been given to them. I have chosen to do this in relation to radiotherapy because of one of the big differences between that form of treatment and chemotherapy. With radiations we can make the effective agents, the ionisations, occur in numbers of our choosing and in the volume of tissue of our selection whereas, with chemotherapy, once the effective agents, the molecules, have been put into the body we have, usually, no control over where they go.

I will therefore take another example from our patients. One had a tumour which measured 73 mm in diameter at the start of treatment and which was resorbed during and after fractionated radiotherapy Our data comprised 24 sets of measurements fitted by an exponential regression line ($p < 0.001$), at the end of which 9% of the volume of the tumour remained (Fig. 5). The treatment consisted of 27 doses of 204 cGy given, usually, five times a week. The estimates of the volume of the tumour from the time of the fifth dose onward fall on the regression line, but not before that time. It happens that this woman had been treated previously with chemotherapy by one of our colleagues and that the tumour was growing in the period immediately before the radiotherapy, so that we have a growth slope with a volume-doubling time of 10.4 days. It is also true that the radiotherapy did not eliminate the clonogenic cell population, and so the tumour grew again, albeit rather more slowly (volume-doubling time = 22 days).

So, we may imagine that the first few doses gradually turned the growing mass into a shrinking one However, after the fifth dose had been reached, the contribution made to the volume by the proliferation of the cells that had survived this dose became negligible in terms of our measurement. No further increment in dose increased the rate of resorption, in spite of the fact that its total was another 4488 cGy. This must have

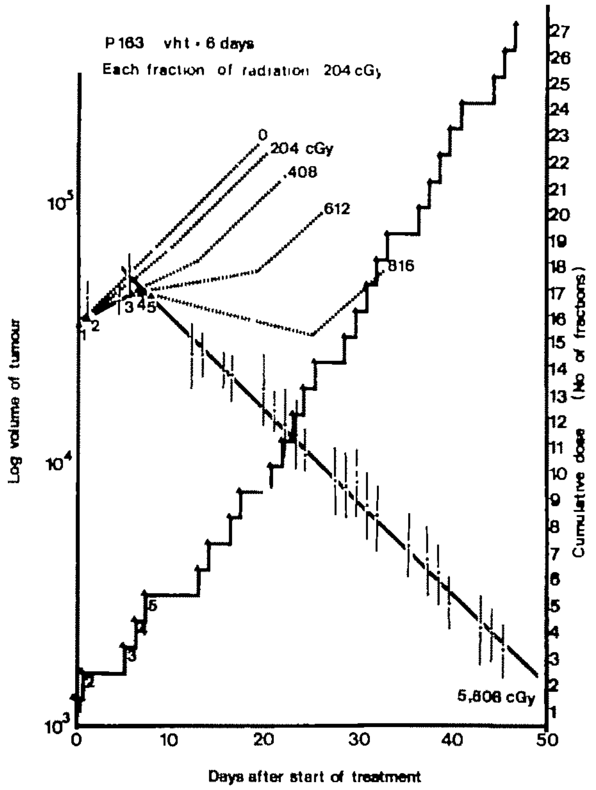

Fig. 5.

Relationship between fractionated dose and resorption of tumour during and after radiotherapy The solid stepped rising line represents the increments of dose (the first five being numbered) corresponding to the number of fractions of radiation (each being 204 cGy) shown on the right-hand ordinate. The solid continuous line fitted to the data points of tumour volume represents the initial enlargement then exponential resorption of this tumour with treatment Before radiotherapy the tumour was growing. The dotted line marked 0 is an extrapolation of the growth curve. The other dotted lines represent what might have happened had only the indicated dose been given.

produced a considerable reduction in the number of surviving cells, even though it did not eliminate the population.

Thus we can say that, once the increments of volume that result from cell proliferation during the intervals between measurements have been reduced to smaller quantities than we are able to detect, the rate at which tumours get smaller is independent of cell-killing and cannot, therefore, be used as an indication of the effectiveness of treatment.

Carcinomas of the human breast treated with radiotherapy become smaller at very different rates. These rates appear to be independent of the size of the tumour at the start of treatment. We have examined this relationship in 148 instances and the coefficient of correlation is 0 04. For convenience we have divided the spectrum of slopes into 10 classes from fast to slow A comparison can be made between the class of slope and the dose of radiation, calculated as "rets" in order to allow for different schemes of fractionation. The coefficient of correlation between the two is 0.02 This is confirmation that the way in which a tumour becomes smaller is not dependent on the treatment that is given once this passes beyond some threshold level of effect.

## Minimum Size After Treatment

Of course, one might try to use the minimal size that a tumour reaches after treatment as a measure of effect But there are four major difficulties in the way of doing this Firstly, human tumours often become too small to measure before they grow again, consequently no minimum can be determined. Secondly, the curve down to the minimum may be very shallow, so that measurement must be repeated on many occasions in order to establish its position. Thirdly, the differences in the minimal sizes, when definite, may be very small and therefore lack reliability for assessing treatment. The last two points are made quite clear from the response of transplanted tumours in animals to graded doses of radiation (Thomlinson & Craddock, 1967). Measurements of an anaplastic tumour that might have been expected to show differences in size corresponding to differences in cell-killing and which did show these differences when assessed by the delay imposed on growth, showed only a difference of 3 mm in minimal diameter after single doses of X rays ranging from 10 Gy to 60 Gy. Fourthly, if a residual core of connective tissue remains, the minimal observable size bears no relationship to the minimal size of the clonogenic cell population. I think these reasons preclude this as a technique of assessing the response of human tumours to different forms of treatment

## Criteria of Response

The UICC classification for assessing the response of tumours to chemotherapy (Hayward et al, 1977) recommends the terms "complete response", "partial response" and "no change", but these all depend on resorption to some arbitrary degree. The time over which this is expected or allowed to take place is not usually specified. It seems that frequently, in practice, all this is reduced to the single expression of "the proportion of patients in whom there is an *objective* response". This, to put it at its mildest, is not sound biology. The results are misleading and therefore positively harmful The system should be abandoned.

But surely, there is only one situation in which we can assert with confidence that there is no response That is, where the growth of the tumour continues unchecked by the treatment. This is difficult to demonstrate since it is not ethical to make the measurements needed to establish the growth rate before treatment is given. The true growth rate, however, may become apparent at a later date. If there be a step in the growth curve, even though small. it is clear that the tumour has responded. The size of the step is then a measure of response (Fig. 6). Indeed, one may sometimes be able to establish what might properly be called a "minimal response" where the tumour continues to grow but at a lesser rate. What is needed is not a measure of the proportion of tumours that do, or do not, respond to some form of treatment but an estimate of the magnitude of the response of each individual tumour to every particular form of treatment.

The use of a different criterion for deciding whether or not tumours respond to particular drugs has important practical consequences. For example, in the largest series of patients that I know of treated with fluorouracil alone, Ansfield et al (1969) reported that 24% of 576 tumours responded, but our experience, using the criterion of a step in the growth curve shows that the response rate of 82 tumours was 100%.

### CELL SURVIVAL AND RESPONSE

In the last resort we are concerned with populations of neoplastic clonogenic cells rather than the size of the tumour. A foundation stone of modern radiobiology is the cell-survival curve. It is now 30 years since Puck and Marcus (1956) published the first survival curve of human cells: the HeLa cells of a carcinoma of the uterine cervix. In therapeutic terms—that is, in terms of attempts to eliminate populations of neoplastic clonogenic cells—the data from which survival curves are derived are, by definition, manifestations of failure. Therefore, the actual failure of treatment in the clinic bears a relationship to some point on a conceptual survival curve of the cells of the tumour in question. If we could only determine this point we should be in a much better position for analysing our failures and for comparing one form of treatment with another. For a few minutes I should like to see where this line of thought may lead.

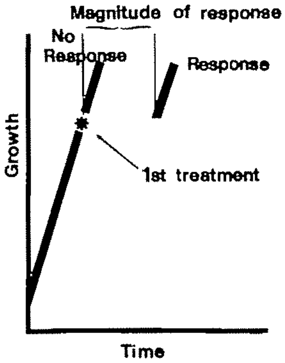

FIG 6.

Only when growth continues through treatment can there be said to be "no response". The magnitude of a step put in the growth by treatment is a measure of the response. The occurrence or not of resorption is not relevant to the magnitude of the response, but it gives information about the tumour

We are not able to measure the number of cells in a tumour that our treatment has killed, nor the number that it has failed to kill. All we can observe are the manifestations of the progeny of the cells that have survived the treatment. Let us imagine to begin with that the proliferation of the progeny results in a tumour that grows exponentially. Let us also imagine two tumours of the same size and structure that have the same growth rate. Then, if we gave each a different treatment such that one resulted in fewer surviving cells than another, we should find that both tumours regrew, but that one appeared later than the other. Our problem in the clinic is that we want to find a new treatment which leaves fewer cells surviving than the best treatment that exists at the present time. Leaving aside other aspects of treatment, such as its side-effects, it would be unethical to try out a new treatment unless we thought it would do at least as well as the ones we have.

At this point I should like to tell you of my personal debt to Professor Silvanus Thompson. In January of this year, 1986, 4 months before I was invited to give this lecture, I had on my desk the drawing from which the slides illustrating these concepts were made and was reading again Professor Thompson's book *The Calculus Made Easy,* when I came across this sentence: "right through the differential calculus we are hunting, hunting, hunting for a very curious thing—a mere ratio". It struck me that, fundamentally, this is exactly what we are wanting to do in all clinical trials in which we are trying to find forms of treatment that kill more cancer cells. I must leave for a moment the line of thought to which I was driven by this sentence.

### A NEW SCALE OF VOLUMES

If we wish to link in our thoughts the progeny of the surviving clonogenic cells and the tumours that we may observe and measure, we need a common scale. In general, we all find it difficult to think in terms of changing volumes. Probably, if I spoke of a tumour as having a volume of 65 000 $mm^3$ it would convey nothing to you at first, certainly less than the idea of a sphere of diameter 5 cm or 2 in. Yet we are nearer to the biological processes involved if we are able to think of tumours changing in volume rather than diameter and it is easiest to think of the rates of change in terms of the time taken to double or halve these volumes.

We have seen that tumours, at least in the breast, grow and shrink exponentially over the range of sizes in which clinical measurements are possible. Though this growth represents the accumulation of a variety of components, it is consequent upon an increase in the population of neoplastic clonogenic cells. This increase may also be exponential. In its simplest form, where proliferation of such a population results in a doubling of cell numbers with each generation, the logarithm of these numbers to the base 2 is a convenient scale with which to describe them.

We are told, first, I think by Collins in the United States (Collins et al, 1956), that a million neoplastic clonogenic cells gathered into a single volume would occupy a sphere 1 mm in diameter, and I think we can accept this as a generalisation. Perhaps, more conveniently, we might say that the volume of a million cells would be 1 $mm^3$, in which case the volume of a single cell would be one picolitre. So if we use the picolitre as our unit of volume and the logarithm to the base 2 as the scale we can cover all volumes from that of a single cell to the largest tumours seen in the clinic in the same terms of size. This scale is very easy to use and to remember. For example, a sphere having a volume of $2^{29}$ picolitres has a diameter of 1 cm. This volume could be called Size 29. Since the volume increases as the cube of diameter each increase of size by 3 means doubling of diameter, Size 32 being 2 cm, 35, 4 cm, and so on. Alternatively, Size 30 which has a diameter of 0.5 in, may be used as a point to remember When this scale is used for the ordinate of a graph showing the change in tumour size with the abscissa calibrated in days, the rate of change in terms of volume-doubling or volume-halving times can be estimated at a glance

The largest tumour of the breast that we have measured in the clinic had a mean diameter of 161 mm. This is Size 41. It is salutary to remember that the smallest tumours that we find in the breast clinically are about Size 29 and by bone scanning or mammography are not less than about Size 25 or 26. If curing patients of their cancers involves the total elimination of the tumours there is still a very long way to go after the volume has been reduced beyond the smallest sizes that can be detected, let alone measured, by our existing techniques.

## A MODEL OF GROWTH

Let us then return to the hypothetical model and examine the pattern of growth of a number of tumours, identical in all respects except that the number of surviving clonogenic cells is fewer in some than in others We could then use the time taken to grow to Size 42, a little larger than our largest tumour seen in real life, as a measure of the differences between the tumours. In this case the ratios of the time taken to grow would be the ratios of the cells surviving in each tumour.

Unfortunately, life is not arranged like this. One of the most important variables in the behaviour of tumours is their rates of growth. If we had a number of tumours identical after treatment, including the number of surviving cells, in all respects but their growth rate and were we to measure the time required by each to grow to Size 42 we should obtain a distribution of times. If, therefore, we wished to resolve a difference between numbers of surviving cells in two groups of such tumours receiving different forms of treatment, we should have to be able to distinguish between two distributions. To attach significance to any difference that we might find we should first have to be assured that the samples giving these distributions were drawn from comparable populations, or, in a special sense, that these distributions had the same "shape". The distribution of times taken to grow depends on the distribution of growth rates The simplest way to establish the comparability is to measure these rates. Because of their variety, the distribution of times taken to grow to a standard size (Size 42) will broaden as the size of the population of clonogenic cells from which the tumour grows again decreases and the total time taken to grow becomes consequently greater. It follows from this that the worst circumstance in which we should seek our "mere ratio" that will express the difference between two forms of treatment is that in which the treatment is highly effective.

We have data concerning 217 primary tumours of the breast from which, by using the rates of resorption as a substitute for growth rate, we can calculate the distributions of times that would be taken to grow to Size 42 on the supposition that each tumour started from any chosen size (Fig. 7). The shape of this distribution is highly skewed and is in fact log normal. The more effective a previous treatment had been, the more doublings of volume would be required before the end-point was reached and the wider would be the spread of the distribution. Though these distributions look different they are, in the special sense used, the same shape, since growth rate is the only variable between them.

From our data it is possible to calculate the sample size, that is, the number of patients that would be required in a randomised clinical trial, to resolve the difference between the distributions with 95% confidence when the true ratio of surviving cells has a given value (Thomlinson, 1986). Were one treatment to leave half as many cells surviving as another and if 32 doublings of volume were needed to reach Size 42, then approximately 6000 patients would be required. To resolve the distributions, were the ratio 1/10 about 600 patients would be needed. These figures result when only one of the many variables, the growth rate of the tumours, is taken into account.

## THE EFFECT OF TREATMENT

The drawings of these distributions were also on my desk when I read Professor Thompson's statement about a "mere ratio" and I realised then that the principle used in the calculus, of seeking the ratio from a little bit of each characteristic, could be applied to different forms of treatment. To do this we should look at the effect of a little bit of treatment and I realised that the method of treatment that we are using, although designed and developed from other reasoning, produced data that permitted this type of analysis.

It is important to emphasise again that, in assessing

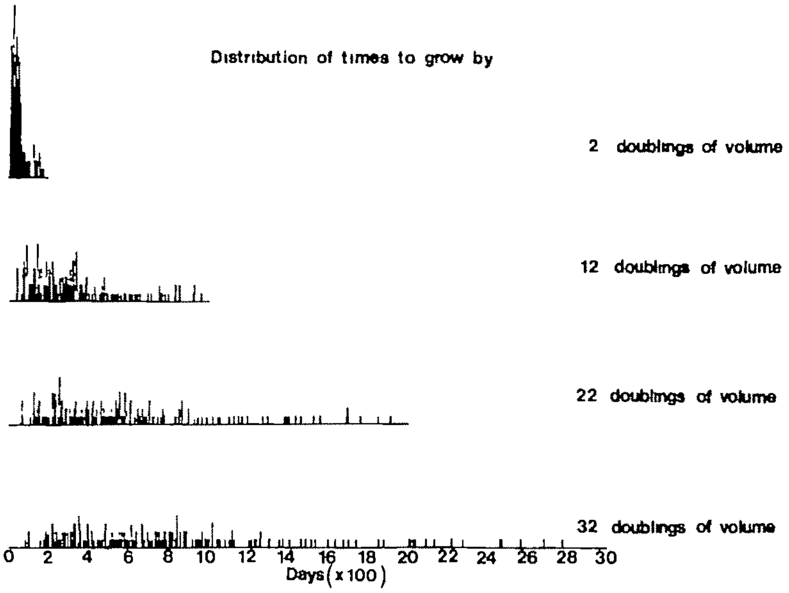

FIG 7.

Distributions of times that would be taken by 217 primary carcinomas of the breast to grow by various numbers of doublings of volume based on measurement. Discrimination between the effects of different treatments depends on establishing a difference in time between such distributions that must first be shown to be of the same shape. The smaller the size from which the tumour regrows, the more difficult to determine any differences in time.

treatments, we have two classes of variable that are of totally different natures and that solutions are less likely to be found by fusing them than keeping them apart. One class involves all the biological differences between tumours, the other, the differences, that may be pharmacological, physical or merely temporal, between treatments. Clinical trials that attempt solutions to both classes of problem simultaneously now have a history that makes it seem unlikely that they will be successful.

There are other variables than growth rate between tumours of the human breast. One of these is the size at the start of treatment. Other things being equal, the smaller the starting size the longer it would take for a tumour to grow to Size 42. We have measurements of 238 tumours of the breast at the start of treatment. These range from Size 30 to Size 41. The distribution of these sizes is also log normal. Since there is no correlation between the size of a tumour when first seen and the rate of growth (as represented by the rate of resorption: $r = 0.04$), the effect of this range of starting size can only be to widen yet further the distribution of times taken to grow to the end-point. Worse still is the effect of cells that might be dormant for an unknown period in a central core of fibrous tissue within a tumour and that might cause it to grow again at some later time—a time which must be highly variable and about which, at present, we have no information. It is because of these variables that the differences between treatments, for example the differences between one cytotoxic drug and another, are unlikely to emerge from trials where the treatment being tested reduces the number of surviving cells to the lowest levels that can be achieved. It is for this reason that I think we should assess the effects of a little bit of treatment, preferably the first little bit, rather than to try to compare the results of a new treatment with those of the best that exist.

I shall postpone telling you, for a little longer, exactly how we treat our patients and the reasoning behind the method. For the moment suffice it to say that we start with a single cytotoxic drug given weekly by intravenous injection for 4 weeks. An example of the consequences of using fluorouracil in this manner may be used to illustrate the method of assessing its effect (Fig. 8). In the first 6 weeks after the start of treatment rather more than half the volume of the tumour was resorbed. After that time, despite treatment with tamoxifen, it began to grow again. When the certainty of this was established—and this involved an increase in diameter of 13 mm—treatment was continued with cyclophosphamide. This resulted in further resorption at the same rate as with fluorouracil.

There are a number of lessons to be learned from this. Firstly, the tumour responded to fluorouracil and also to cyclophosphamide, but not to tamoxifen. This information was gained quickly. Secondly, the response, or lack of it, to tamoxifen could be determined without an open biopsy and with certainty. Since only about one in three tumours does respond and since tamoxifen costs about £1 per person per day and since there is no point in continuing with a useless drug, however minor may be the complications of its use, this is valuable information. Thirdly, since the rate of resorption, with adequate treatment, reaches a maximum that is characteristic of the individual tumour and since the rates of resorption after fluorouracil and after cyclophosphamide are equal, it is likely that the dosage of each of these drugs was adequate. This is a point to which we must return later. Fourthly, the effect of these drugs can be estimated quantitatively. Here I will

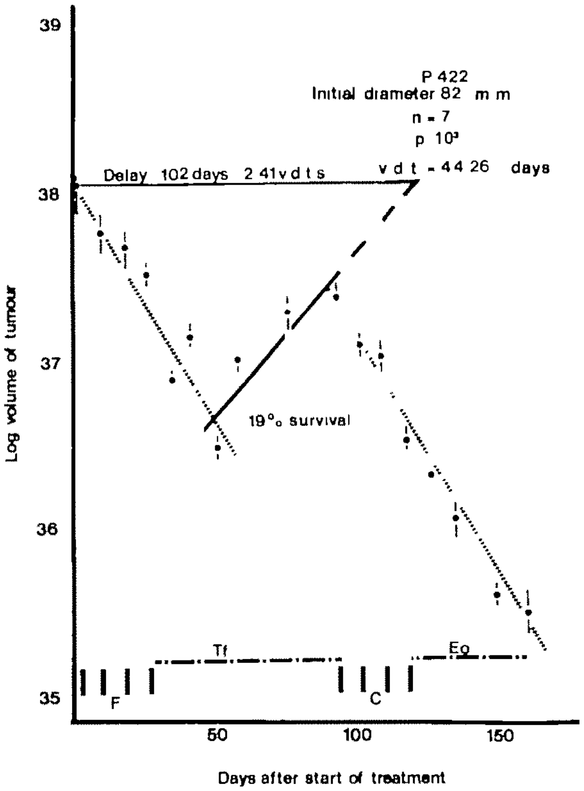

FIG. 8

Pattern of response of a carcinoma to four injections of fluorouracil (F), oral tamoxifen (Tf) and cyclophosphamide (C). The fluorouracil induced a delay in growth of 102 days which is 2 41 times the volume-doubling time of the particular tumour This is "as if" 19% of the cells had survived and doubled 2 41 times to re-establish the original size.

confine myself to the fluorouracil. This clearly delayed the growth of the tumour. The growth slope of the tumour can be used in this case, by extrapolation, to calculate the time by which the growth was delayed. Rather than use the time taken by both untreated and treated tumours to grow to Size 42, the delay has been calculated for the time at which it would have reached its original size. This method diminishes errors introduced by extrapolating a line that already carries its own standard deviation. By using this standard, allowance is also made for the differences in size of tumours at the start of treatment. In this way a value of 102 days was calculated for the delay imposed on this tumour by four injections of fluorouracil.

The duration of the delay depends in part on the growth rate of the tumour. In this particular case we can estimate the volume-doubling time from the growth slope of the tumour as being 44.26 days. By dividing the delay by the volume-doubling time we conclude that a delay of 2.41 volume-doublings resulted from the treatment. This measure of effect is now independent of both the size and the growth rate of the tumour Tentatively, we can go one stage further. Had we delayed the growth by one volume-doubling time the tumour would have behaved as if 50% of its clonogenic cells had survived. I am not asserting that 50% of the cells would have survived, but that the behaviour of the tumour would be "*as if*" this were so. We can therefore talk of a quasi-surviving fraction, by analogy with Dr Alper's "$D_q$" (Alper et al, 1962) In this particular case with 2.41 volume-doublings of delay, it is as if 19% of the cells had survived.

Another patient provides an example of two added problems associated with the method that are general. In a similar manner she was given four injections of fluorouracil followed by tamoxifen, to which she appeared to respond. Resorption of the tumour continued with a single exponential regression line describing the reaction to both treatments. One problem is that we have no growth curve; the other, that we do not know for how long the fluorouracil continued to be effective after the last injection. We are able to define a lower limit to the effectiveness of the drug by using the slope of the regression line for resorption as a substitute for that for growth and by extrapolating from the first day on which a new treatment is given. In this way the calculations used in the previous example can be repeated but the effect of the drug is almost certainly greater than these would suggest.

Experience has shown that it is probably valid to make this extrapolation from a point on the regression line of the resorption resulting from a treatment corresponding to 1 week after the last injection. In a preliminary investigation, the statistician has applied these criteria to 82 patients whose treatment was started with four injections of fluorouracil. Each calculation is likely to be an underestimate of the effect of the drug, but a histogram of the distribution of the "quasi-surviving fraction" of cells (Fig. 9) shows that all tumours responded It is a highly skewed distribution but more than 50% of patients have less than 30% of cells surviving.

To have reduced the proportion of clonogenic cells in a tumour to around 30% of the starting value is very little in terms of eliminating the population, but this is a test of a drug, not of a form of therapy, and a drug being used as a starter to the whole treatment. The test not only gives a quantitative assessment of the drug but also some indication of how valuable it is for each particular patient.

We have fewer data on other agents used for first courses of treatment but the principles can be applied wherever a treatment can be shown to have put a step in the curve representing the growth of a tumour by inducing some delay.

## A DOSE–RESPONSE CURVE

The validity of this method of assessing the effect of some small portion of a scheme of treatment gains

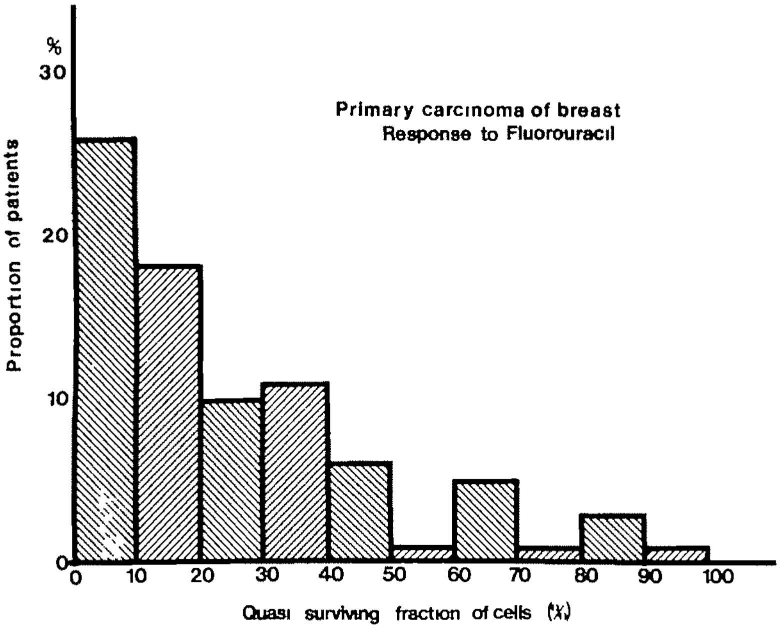

FIG 9.
The proportion of 82 patients treated with four injections of fluorouracil whose tumours behave *"as if"* various fractions of their tumour cells had survived.

support from unique data based on sets of measurements made on 90 occasions over a period of 2.5 years. A patient presented with a tumour 118 mm in diameter, Size 39.6 on our scale. She was treated by one of our colleagues using weekly injections of a combination of fluorouracil, cyclophosphamide, vincristine and methotrexate. Later she had two courses of radiotherapy, to one of which I have referred (Fig. 5). In four separate periods she had courses of this combination of cytotoxic drugs, receiving always the same doses but 16, seven, two and four injections respectively in the four courses.

Each course induced a period of delay in the growth accompanied by some resorption of the tumour (Thomlinson, 1986). The number of volume-doublings of delay induced by each set of injections can be used to construct a dose–effect curve (Fig. 10). A straight line passing through the origin, as it must, is a good fit to the data (the coefficient of correlation is 0.995 and $p$ is much less than 0.001). Were this method of assessing the effectiveness of treatment invalid, it is improbable that such a result would have been obtained.

It would be possible, on the basis of calculating the "quasi-surviving fraction" to deduce some sort of cell-survival curve from the "dose–effect" data. Without more knowledge of the clonogenic cells and their behaviour this would only be playing with numbers. However, with the advent of new methods, particularly image analysis and the possibility of estimating the number of tumour cells in cycle from biopsy material, there will come the real possibility of estimating the effect of treatment in terms of the fraction of neoplastic clonogenic cells that survive. The effect of the first course of injections could have reduced the surviving fraction to less than $10^{-9}$. This is consistent with the tumour's being impalpable for about 150 days. Perhaps only a few hundred cells were left and, since the tumour had not spread, the patient must have been close to being cured. This situation did not recur with her subsequent treatment.

## CAUSES OF FAILURE

Why then do we fail? In trying to answer this question we must go back to a much bigger scene, to the whole spectrum of breast cancer and, indeed, to cancer as a whole. While I would like to consider all forms of cancer in principle, my illustrations will again largely be drawn from cancer of the breast and the principles that I suggest would need modification to suit other particular situations.

In October 1986, on the morning of Lord Scarman's re-visit to Brixton to observe the effects of the recommendations he made after the riots, he appeared on the BBC's Breakfast Television and included a memorable sentence in his remarks. He said "You have to direct the therapy to where the disease really is". In the last 50 or more years treatment of carcinoma of the breast has given a 20-year survival rate of about 20% (Forrest, 1986) About four out of five patients have died of metastases. In the case of mastectomy the metastases must have been present at the time of surgery and probably for some time before. Radical mastectomy removes, on average, about 1% of a woman's body. This 1% generally does not contain all the neoplastic cells. The therapy is not "directed to where the disease really is". So in the case of surgery the explanation of failure is easy to find

Radical radiotherapy for carcinoma of the breast

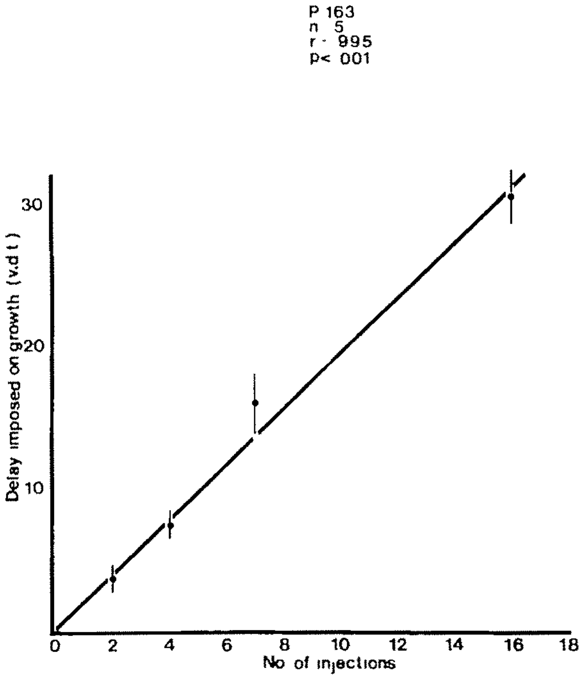

FIG. 10.

Dose–response curve relating the number of injections of a combination of cytotoxic drugs given per course to a single patient, and the response of the tumour expressed as the number of volume-doubling times by which growth was delayed by each course

may reach 3% of a woman's body. Success within this field is not certain, but the fact that post-operative radiotherapy has not been shown to improve the rate of survival resulting from surgery alone indicates that the major problem is the same: that of disseminated disease.

Only a few types of human tumour are susceptible to influence by manipulation of hormones. Carcinoma of the breast is one of them, but only about one in three tumours responds. The effects of these would seem to be to enhance the power of the signals normally controlling proliferation to limit the activity of some neoplastic cells, but they seem to limit that activity rather than to eliminate the population.

So, we are left with the cytotoxic drugs. Why do they fail? Obviously, in order that they should work, they must be directed to the place "where the disease really is". But how? I think that no one would dispute the concept that the best time at which to attempt to eliminate any population of neoplastic clonogenic cells in a colony is when it is at its smallest. But when the colonies of cells in metastases are small we do not know where they are, let alone their size, for the smallest that we can localise at present is several sizes upward from Size 23, and that would have a diameter of about 2.5 mm.

New techniques, such as magnetic resonance imaging, are already with us. Others, such as radioactively labelled monoclonal antibodies, are just round the corner. I hope that the scientists of your Institute will help to develop the collection of quantitative data by these and any other new methods but I am afraid that this will not happen until doctors looking after individual patients insist upon it. Meanwhile we must continue with our blunderbuss methods. On occasion, cytotoxic agents may be infused into the artery supplying the lesion. This presupposes knowledge of the site and extent of the lesion, but anyway has its own hazards In general, we give intravenous injections and, from the moment the molecules enter the bloodstream, we have no further control of, and little knowledge about, their destination.

### THE DISTRIBUTION OF DRUGS

The distribution of these molecules must be related to blood flow This we may consider firstly in relation to the organs of the body and secondly in relation to any tumour within an organ.

It is interesting to note that in the last 5 years we have not seen a patient develop metastases in the lung while undergoing our form of treatment, but we have seen them develop in liver and bone. Lung is the third commonest site, after liver and bone, for metastases from cancer in the breast and, on statistical grounds, we should have expected to see some. Why have they not appeared? The drugs are carried from the veins to the heart and the whole of the output of its right side goes through the lungs. Since these are about 1.6% of the body weight and receive practically the whole dose, the tissue concentration is likely to be high. Only 4% of the output of the left side of the heart goes through the hepatic artery to the liver, which is about 2% of the body weight. Eighty per cent of the blood flow to the liver comes through the portal system but this blood has passed through the capillary network of the alimentary tract. So, it may well be that the liver receives only about 4% of the quantity of drug in an injection. This is surely not irrelevant to the difference in incidence of metastases that we have observed. That this cannot be the whole truth is evident from the fact that the nutrient arteries to bone are smaller still and that we can get enough drug into the bone marrow to do severe damage to the haemopoietic system without being able to eliminate or prevent the growth of metastases in bone. We must, therefore, consider the circulation within the metastases themselves.

The liver is a common site in which metastases grow and frequently a range of sizes, and therefore of ages, may be seen in a single organ. In these metastases, changes representing a sequence of developments in their internal circulation may be seen. Except where the metastases impinge on the capsule of the liver or one of the larger vessels or on one another, they tend to be spherical. When they are "small", an equatorial cut surface has a rather homogeneous appearance. In this context "small" means up to about 8 mm in diameter, though this may vary from one type of tumour to another.

As each metastasis enlarges, the total size of the capillary bed within it must increase and the relevant arteries and veins are displaced further and further from the centre. The enlargement of the capillary bed, relative to the bore of the vessels that fill it, must lead to a tendency to slowing of the average flow of blood in the capillaries. However, the length of the intracapillary pathway of blood reaching the centre of the lesion is longer than that of the blood at the periphery. Were all else equal, this would result in greater resistance to the flow of blood to the centre and an uneven distribution of the rate of flow within the capillary bed, with more slowing towards the centre.

It has been shown in experimental preparations of growing tumours that the first of a sequence of visible changes leading to necrosis is dilatation of capillaries (Rheinhold, 1969). In equatorial slices through metastases in the liver, a pink flush can be seen in the centre of slightly larger examples, for example, those 9 mm in diameter. With further enlargement the flush spreads and becomes a ring (Fig. 11). Within the ring the tumour cells have died and, as in an infarct, their swelling in this process has squeezed the blood out of the still-patent vessels. Explanation of this sequence of appearances indicates a progressive slowing of the circulation leading to malnutrition of cells. This explanation also implies the delivery of progressively lower concentrations of cytotoxic drugs to the central parts of these tumours. This would be of no consequence were every cell affected in this manner to die of malnutrition. In the analagous situation of the delivery of oxygen, it has been shown that, after treatment, some cells do survive in comparable experimental situations and are able to grow the tumours again (Thomlinson, 1977).

In the more slowly growing metastases, connective tissue and collagen form as the tumour grows. We have an example of such a metastasis from carcinoma of the breast growing in subcutaneous tissue. This responded to our form of treatment but started to grow again in any interval between courses of injections and so for this reason it was excised. The circulatory changes and death of cells take place more slowly in such tumours and some intact neoplastic cells can be found, usually associated with blood vessels, with the condensation of collagen fibres that occurs in the centre.

Neoplastic clonogenic cells that have come to be in such a position may well survive the deterioration of the nutritional state when treatment prevents further growth of the tumour. They may well also survive the injections of cytotoxic drugs if these are all given while the local circulation within the tumour is poor. In carcinoma of the breast, I think that this story is the explanation of the commonest and most important single cause of the failure of cytotoxic therapy.

The sequence of events, as we understand it, may be summarised simply. Cytotoxic drugs reach the periphery of the tumours in concentrations sufficient to cause the death of many clonogenic neoplastic cells. If the surviving population is of negligible volume in terms of the system of measurement being used, the tumour will shrink at its maximal rate, this being determined by the composition of what remains. In the early stages the main component is likely to be the population of non-clonogenic, *i.e.* well differentiated, tumour cells whose members die at the end of their natural life-span and the material of which they are made is then resorbed. In the later stages the main component will be collagen with a volume-halving time of the order of 5 months. Among the collagen fibres in the central part of the tumour will be a few neoplastic clonogenic cells that have survived the local malnutrition, perhaps by chance, and have survived the treatment because of the poor local blood flow. As resorption continues, any of these cells that come to lie

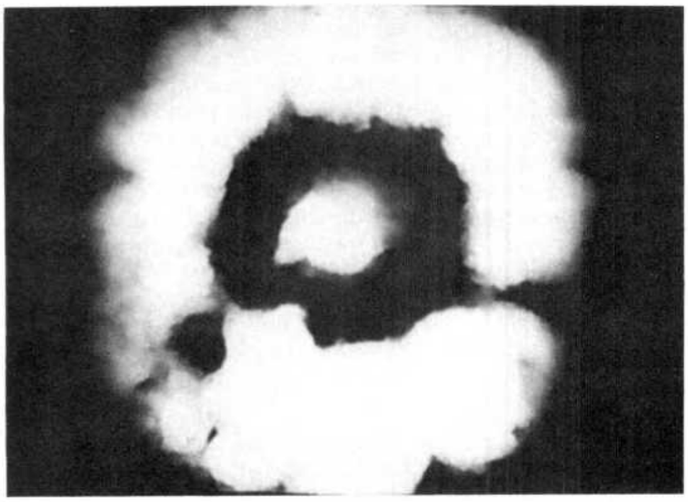

FIG. 11.

Photograph of the cut surface of a liver bearing metastases. The pale area is the equatorial plane of a metastasis 14.2 mm in diameter. The dark ring is a zone of dilated capillaries and the lighter centre is necrotic tumour tissue.

near the edge of the tumour as it recedes toward the centre are likely to become better nourished, to proliferate and to cause the tumour to grow again

Certainly we see approximately spherical tumours become smaller exponentially with time until there is a residuum in which we measure little change until we are aware of its enlarging again with an irregular nodular form. Of course this type of observation and our experience of a unique response of a tumour that shrank and regrew repeatedly (Thomlinson, 1982) does not amount to proof of this hypothesis concerning the failure of chemotherapy, but there is so much evidence that the probability of its being correct is too high to be ignored.

Re-stated briefly, this hypothesis is that the therapy does not get to where the disease really is because of the condition of the local circulation.

### "Resistance" to Drugs

I am not suggesting that this is the only reason for the failure of chemotherapy We can learn something of others from our measurements. Over and over again we find that the regression lines resulting from chemotherapy are parallel to those from radiotherapy. This would seem to indicate that the drugs are getting to the tumours in effective quantities. But sometimes this is not so and then we might question the dosage Occasionally, however, our measurements show a dramatic change in the behaviour of a tumour without there being any alteration in the treatment being given. This change is the renewal of growth of a tumour whilst the treatment that had previously lead to resorption was being continued. I shall illustrate this with three examples of patients being treated in different ways by some of our colleagues

In the first example of this kind, 65% of the volume of a tumour was resorbed while the patient was being treated with stilboestrol and cyclophosphamide given orally. Then the tumour started to grow and radiotherapy was given. This resulted in a further period of resorption described by a regression line parallel to the earlier one. One must ascribe the growth to the proliferation of cells that were "resistant" to the drug

In another example a tumour responded to nine injections of fluorouracil which, in terms of the "quasi-surviving fraction", had resulted in the death of about 80% of the cells and was accompanied by resorption of more than half the volume of the tumour However, the tumour then started to grow again and continued, despite a further four injections of fluorouracil It then responded to a mixture of cyclophosphamide and vincristine

In the third example a similar sequence of events accompanied combination chemotherapy with a mixture of cyclophosphamide, vincristine, fluorouracil and methotrexate. Again, growth became apparent after the ninth injection.

In each of these tumours there could have been a subpopulation of cells that was resistant to the drugs involved before they were given, but the evidence makes it more probable that the resistance was induced by the drugs For this to happen, the cells must have met the drug concerned and survived the meeting, that is, it reached them in sublethal concentrations. This is most likely to happen in the central regions where the flow of blood is poor.

There are, however, other patients whose tumours do not respond to a particular cytotoxic agent even on the first occasion that it is used. We have observed this more often with adriamycin than with any other individual drug, but have also seen continuing growth after cyclophosphamide, vincristine or mitozantrone. The number of these instances is too small to have any statistical significance, but it is important to be aware both that this can happen and that the phenomenon may be masked by the use of combinations of drugs In instances where it has happened the tumours have responded to other cytotoxic agents, so that it is more probable that the absence of response is related to some inherent "resistance", whatever this may mean, than to underdosage.

Not all tumours, however, show evidence of "resistance", be it inherent in some of the cells from the start or acquired by adaptation and natural selection in a changing environment. The patient from whom we calculated the dose–effect curve (Fig 8) is a case in point. The straight line through the origin and the data points would have been a good fit even if there had not been the second point on the line, representing the effect of four injections. But this represents the effect of the fourth course of treatment given some 650 days after it all began. During this time 25 other injections of the same combination of drugs had been given. The tumour was initially very large, a fast grower, with a volume-doubling time of 10 days. It had grown again after each of three courses of cytotoxic drugs and after a large dose of X rays. Yet the dose–effect curve shows that it responded to the 26th to 29th injections in exactly the same way as it did to the first course. The cells that survived all of the previous treatment had not become resistant to the combination of drugs

Finally, amongst the prominent causes of failure, we must consider the dose. Apart from other factors this should be related to the rate of proliferation of the clonogenic cells of the tumour and of the limiting normal tissues, usually the bone marrow. Occasionally, in perhaps 2% of patients with carcinoma of the breast, damage inflicted on the haemopoietic system and the very rapid growth of the tumour, make it impracticable to introduce sufficient cytotoxic drug to prevent the continued expansion of the population of neoplastic clonogenic cells. It is important, by accurate measurement, to recognise these patients at the earliest possible time and to institute some other form of treatment immediately.

### Rationale of Treatment

In the light of this background, I can summarise the rationale for the way in which we treat our patients

Whatever method might be chosen for attempting to eliminate a population of clonogenic cells in a patient, the probability of success is bound to be at its highest when the size of the population at any one site, be it in a primary or secondary tumour, is at its smallest. The results of treatment over the last 50 years indicate that in some four out of every five patients there were neoplastic clonogenic cells in parts of the body that were not included when localised treatment had been given. Although careful selection does increase the chance of all clonogenic cells being removed by surgery, selection for this criterion cannot be made with certainty. Breast cancer should therefore be treated from the start as a disease of multiple lesions, except where there is sufficient evidence to justify the treatment of only one. It follows that when the aim of treatment is the total elimination of the neoplastic clonogenic population, that is, the cure of the patient, cytotoxic therapy should be the form of treatment used at the start.

If the principal reason for the failure of chemotherapy is inadequate delivery of the drugs to some parts of tumours because of the poor local flow of blood, the aim of the early stages of treatment should be to kill as many cells as is easily possible so that the probability of further growth and spread is diminished and, because of the resorption of the material composing the tumour, the flow of blood to the remaining parts is improved. Once an adequate proportion of the clonogenic cell population of a tumour has been killed, the lesion gets smaller at its own rate which is not increased by larger doses of treatment. Therefore, the right dose at the start of treatment is the smallest that causes the particular tumour to become smaller as quickly as it will. This effect can be achieved with any of a number of single cytotoxic agents. A by-product of this use of the drugs is the very much reduced incidence and severity of unpleasant side-effects in comparison with the standard regimes.

Because the rate of resorption is a characteristic of each tumour but with a wide variation from tumour to tumour, it may take a long time, sometimes several years, for the process to reach completion, that is, to reach Size 0, not Size 25 or whatever is the smallest that can be detected. It is possible that at any time during the process an improved blood flow may reach the neighbourhood of malnourished clonogenic cells, enabling them to renew their proliferative activity. Consequently, the probability of eliminating these cells will be increased if therapy can be maintained throughout the period. However, the continuation of treatment with any single agent, or combination of agents, for long periods of time is likely to lead to adaptation by the clonogenic cells thence to "acquired resistance" of the tumour and continued growth. For this reason we have chosen to give only four injections of any one agent, given weekly for want of knowing better, and then to make a change.

The benefit to the patient of any dose of cytotoxic drug is likely to last for a finite but unknown period of time after it has been given. The relevant argument is between the rate at which the surviving clonogenic cell population may increase and the rate at which its erstwhile "protected" members become accessible to the next dose because of continuing resorption. We have arrived at an interval varying between 2 and 6 weeks, depending on the volume-halving time of each tumour. Clearly, any upward deviation of the size of the tumour from the regression line describing its resorption indicates a change in the situation.

About one cancer of the breast in three responds to therapy with hormones. The action of these is to inhibit proliferation rather than to kill clonogenic cells and is therefore complementary to that of the cytotoxic drugs. Effective therapy with hormones should result in a continuation of the process of resorption. In the interval following the first four injections of a cytotoxic agent we therefore give one of the hormone preparations, usually tamoxifen. An upward deviation from the regression line indicates a lack of response and then the administration is stopped. In the absence of this evidence the hormone treatment is continued until there is some other indication for a change of management. In other intervals between sets of injections of cytotoxic drugs other hormone preparations may be tried if tamoxifen has not helped.

After an interval appropriate in length for the response of the individual tumour, cytotoxic therapy is continued with four injections of a different drug and then the process is repeated. We normally use fluorouracil, cyclophosphamide, vincristine, methotrexate, doxorubicin and mitozantrone, though not necessarily in that order. Occasionally we have used vinblastine and epirubicin. By using these drugs in sequence we have covered periods approaching 1 year and have shown that they can be used effectively in a second cycle after this We have called this form of treatment "measurement-based sequential therapy" (MBST).

Sometimes we are left with a residual tumour that does not become smaller and we think it right that this should be excised. Generally it has proved to be a mass of fibrous tissue with some optically intact neoplastic cells within it and often there is evidence that they have started to grow the tumour again. Surgery is likely to continue to play an important part in the management of this disease for as far ahead as we can see but it is the surgery that is adjuvant, "helpful" to the main management with systemic therapy.

It has been pointed out that as long as the primary tumour remains in place there is a risk of metastasis formation. This must be so, but in terms of cure the risk is important only if it is the first occasion on which a metastasis is being formed. We have to weigh the likelihood of this occurrence in the presence of a treatment to which the primary tumour can be observed to be responding against the advantages of surgery. Excision involves the loss of a monitor of the effectiveness of systemic treatment. In the majority of patients the probability of cure will, in the future, largely depend on the efficiency with which this form of treatment can be given. Consequently a monitor of its effectiveness is of major importance

I would not have you think that we have pursued this form of treatment solely to gain information. When we started it we believed that we were offering the most rational and best treatment for each patient that we knew how to give. Since then, each visit of every patient has been a new occasion for re-assessing what we believed to be in the patient's best interest. That interest has always taken precedence over the possible value of a scientific investigation. Anyway we reckoned that, by making our measurements, we were in a position to learn whatever policy of treatment was being advised We are not making claims to having given a better form of treatment than others, but to having devised a method which is rationally based on simple principles of biology and pathology as we understand them to apply to tumours. The method has far less severe side-effects than most forms of cytotoxic therapy and is acceptable to patients. From it we have gained valuable data on which future developments may be based. Our treatment, which we regard in no sense as definitive, is at least no worse in its long-term results than others.

We have not done a randomised clinical trial because, at this stage, it would have been neither logistically possible nor scientifically appropriate. We can only compare the effects of our treatment over the last 5 years with that given in more conventional ways to the patients whom we could observe in the period before this

As I have made clear, we do not think "survival time" is a good measure of the effectiveness of a form of management but we have been pressed to express our results in these terms. However, we have modified the methods of deriving these times so as to take account of the size of the tumour at the start of treatment and its growth rate. We have calculated the time that tumours of particular size and growth rate in the different patients would have taken to grow to Size 42 without treatment, and then the number of doubling times of their own tumours by which each patient has survived after this point would have been reached.

These data have been submitted to life-table analysis (Fig. 12) The difference between the sets of data is rather less in our form corrected for size and growth rate than in the crude survival data, but in both cases is statistically highly significant and suggests that in each of the 6 years after the start of treatment about 15% more of the patients are alive. We should not lay much emphasis on these results but I think it very unlikely that attempts to eliminate the differences that actually do exist between the groups of patients by means of a randomised clinical trial would result in our form of treatment appearing to be the worse.

It would therefore seem to us to be ethically justifiable to extend this type of treatment and this form of investigation because of the quality and quantity of information that results and which allows analysis of the causes and mechanisms of failure. If, in all fields of cancer therapy, we can learn to eliminate these failures we may cease to be anxious about the rates of our success.

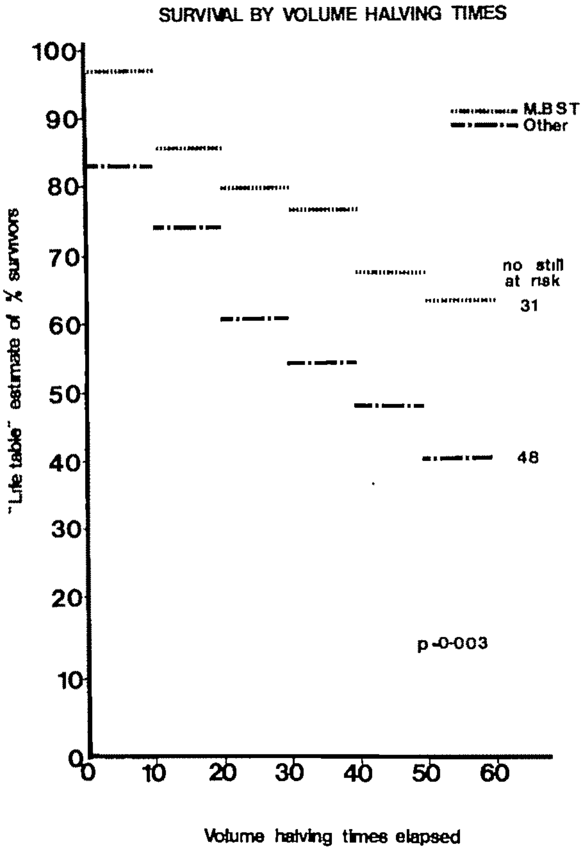

Fig 12

"Life-table" data expressing the probability of survival of patients for a period of time after treatment with single cytotoxic agents given sequentially according to measurements of the tumour (M B S.T. "measurement-based sequential therapy") and after other forms of standard treatment used in the same hospital The unit of time is the volume-halving time of each tumour taken as being equal to its own volume-doubling time The time "elapsed" is after the particular tumour would have reached Size 42 had no treatment been given

Acknowledgments

The work underlying this lecture has been shared with Dr Ann Johnson, without whose collaboration it would not have been possible We are grateful to Mr David Cheung for his advice and handling of the statistical data. The more recent work has rested on the support and co-operation of surgical colleagues, Mr J E L Sales and Mr S J Cox, and for the earlier work we are grateful to colleagues in the Regional Radiotherapy Centre at Mount Vernon Hospital who allowed us to make measurements of tumours in their patients. We are also grateful to all the past and present members of the staff of the Breast Study Centre at Mount Vernon and to a committee of patients on whose financial support the continuation of our work has depended

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# Book reviews

*Breast Cancer. Treatment and Prognosis* Ed. by Basil A. Stoll, pp x+377, 1986 (Blackwell Scientific, Oxford), £39.50.
ISBN 0-632-01485-7

There have been many books published in the last few years dealing with all aspects of breast cancer. These have ranged from simple accounts for the public to highly technical works on the fundamental problems of malignancy and details of research in tumour biology and histopathology.

It is difficult to know just where this new book slots in. Basil Stoll, who has edited this new book, claims that it examines, in a critical and realistic manner, the end-points we are aiming at in treatment, the chance of achieving them, the price to be paid by the patient and the prospects of more effective treatment likely to become available in the foreseeable future. This seems to be a fair appraisal.

The chapters in the first section give good overviews of the much debated issue of "cure", and of the roles of surgery, radiotherapy and systemic therapy. The difficulties of randomised trials are aired and consideration is given to decision-making in primary and palliative treatment. The final chapter in this section describes the psychological impact on the patient of the diagnosis and treatment, and makes sensible recommendations. Not all clinicians will agree with all the opinions expressed, but I think they would gain by reading these chapters.

Section 2 is devoted to prognostic indices. It covers all aspects and provides a clear picture of the present state of knowledge in this area, bringing together the varied factors involved. The picture which emerges confirms the extraordinary heterogeneity of breast cancer.

Section 3 has seven chapters which describe new approaches in research that may produce advances in treatment. Targeting of systemic agents, restraint of metastatic growth and tumour maturation induction are three of the subjects chosen.

The book is well produced, well written and edited with excellent, up-to-date references. It provides a comprehensive and first-class overview of the present position regarding our understanding of breast cancer, our aims in treating the disease and the methods of treatment currently in favour. It leads on to the fundamental issues being researched and indicates areas where improvements in our understanding of the disease may lie and how improvements in treatment may develop.

This book is not for the general public nor for the highly technical laboratory worker. It is an excellent state-of-the-art review covering a wide range of subjects related to all aspects of breast cancer. I think all clinicians with an interest in breast cancer would find much in this book and would have an up-to-date account of present thinking on the disease and its management, with a look into the future.

It fills a gap in the market. It seems reasonably priced and should be available in all departments dealing with breast cancer. I can recommend it to individuals and to departmental libraries.

D. BRINKLEY

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*Cancer in Children. Clinical management. 2nd edit.* Ed. by P. A. Voûte, A. Barrett, H. J. G. Bloom and I. Lemerle, pp xviii+365, 1986 (Springer-Verlag, Berlin) DM78.
ISBN 3-540-15342-X (Berlin)
0-387-15342-X (New York)

The second edition of this very readable book is somewhat expanded and has some new chapters and new authors. It is divided into two major sections. General Chapters and Special Chapters, the former covering aetiology and epidemiology, oncogenes and chromosome aberrations, pharmacology, chemotherapy and radiation therapy, surgical oncology, infections and supportive care, delayed consequences of therapy, clinical trials and a final chapter in this section on paediatric imaging.

There is an inexplicable lack of a chapter devoted to the pathology of childhood tumours, which was present in the first edition and served to emphasise the great importance of accurate histological diagnosis in the subspecialty. The numbers of pathologists really competent to report on childhood tumours are few and, in view of the major advances in subcategorising these malignancies by the use of newer techniques, thus allowing for more accurate prognosis to be established and treatment to be tailored to particular groups, this is a major gap in the book, except in some special chapters where it has been discussed by individual authors.

The chapters on oncogenes and chromosomal aberrations and on radiation therapy are excellent introductions to two areas which are often ill understood. In the chapter on supportive care, the section on psychological care is somewhat brief and omits any comment or advice on the problems of siblings of children with cancer. Meadows and Silber have written an excellent chapter on delayed consequences of therapy, but this has not been complemented by one on treatment for those problems where it is available. This is a particularly worrying omission, as early monitoring and appropriate replacement therapy are essential if unremedial problems are not to arise.

The second half of the book is devoted to chapters on individual diseases and covers all the common and uncommon childhood malignancies, some benign tumours and histiocytosis X, more recently renamed Langerhans' cell histiocytosis. The actual information in the chapters varies a great deal; some are dogmatic and discuss the authors' own methods of therapy with very little reference to other well accepted regimes, while others are an attempt to cover the present ideas regarding optimal therapy. Overall, however, the authors have achieved a well written, sensible account of the current methods of diagnosis and management. They do reflect treatment and results achieved in major centres where modern methods of diagnosis and supportive therapy are available and it would be dangerous for individuals without these facilities to try to emulate the treatment strategies.

This book can be recommended to junior doctors working in the oncology field, whether they be training in radiotherapy, haematology, surgical or medical oncology, and to consultants interested in cancer in childhood, but it should encourage everyone to ensure that children are referred to appropriate major centres in order to benefit from the treatments advocated.

P. MORRIS JONES

1987, *The British Journal of Radiology*, *60*, 753–760 AUGUST 1987

# Improved external beam radiotherapy for the treatment of retinoblastoma

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*(Received December 1986 and in revised form February 1987)*

ABSTRACT

An applicator attached to a 6 MV linear accelerator has been adapted to produce a well defined beam for the treatment of retinoblastoma. By using a contact lens as the reference point on the patient's cornea, the beam edge is aligned to just behind the posterior margin of the crystalline lens, thus sparing the anterior chamber and lens from the radiation field. In addition to basic dosimetric measurements made using an ionisation chamber and film densitometry to quantify the output and dose distribution from the applicator, extensive use was made of thermoluminescent dosemeters and a tissue-equivalent anthropomorphic head phantom This was designed for detailed dosimetry on the eye and was used to confirm the correct positioning and reproducibility of the clinical set-up. We present data that corroborate and extend the dosimetric analyses documented in an earlier Dutch publication In addition to the improved dosimetric analysis, other advantages include patient immobilisation, anaesthetic procedure and finer couch control as well as a recommendation on the dose prescription.

Retinoblastoma is a rare ocular neoplasm arising from embryonic photoreceptor cells in the eye. It accounts for 3% of all paediatric tumours, usually affecting children in the first 2 years of life. Initially, enucleation was the mainstay of treatment for this tumour. In 1929, Foster Moore and Scott at St Bartholomew's Hospital pioneered the treatment of retinoblastoma with radiotherapy using an interstitial implant and adaptations to this technique were later reported (Moore et al, 1931; Innes, 1964). Stallard (1952a, b) predicted from histological examination that a minimum dose of 3500 cGy in 7 days was required; ophthalmic applicators were designed, first using radium and later cobalt 60 (Innes, 1964). Reese and Ellsworth (1964) devised a classification to help define treatment policy, prognosis and comparison of results. External beam irradiation techniques were developed to treat retinoblastoma in an attempt to preserve some useful vision (Skeggs & Williams, 1966; Cassady et al, 1969; Abramson et al, 1981), even to the extent of using a second course of external beam radiotherapy in patients with locally advanced disease (Abramson et al, 1982). From this centre, Bedford et al (1971) reported cure rates of 100% in Stage I and II cases, 86% in Stage III and 75% in Stage IV and V cases, with an overall cure rate of 90%. In advanced disease (Stages IV and V), Abramson et al (1981) have more recently reported a 5-year survival of 88%. The St Bartholomew's Hospital data clearly demonstrate that choroidal invasion and involvement of the optic nerve are poor prognostic signs (Hungerford et al, 1986). With such a good overall prognosis, the preservation of vision has become all important, and thus cryosurgery, photocoagulation, radioactive eye plaques and external beam radiotherapy treatment techniques have been employed and elaborated.

Both radioactive surface applicators and external beam radiotherapy may cause ocular complications and these have been fully discussed by Haik et al (1983). Following early studies employing 250 kV X rays and a minimum dose of 7000 cGy to the whole eye, radiation damage was the commonest cause of loss of vision (Reese et al, 1949). Although the total whole-eye dose delivered for retinoblastoma now rarely exceeds 4500 cGy of conventionally fractionated radiation, cataract is still an important side-effect of external beam radiotherapy, although amenable to surgery. Loss of vision from radiation chorioretinopathy is infrequent with total doses below 5000 cGy and adequate fractionation. When the whole eye is irradiated, corneal vascularisation and opacities resulting from a combination of reduced tear production and corneal exposure due to lid shrinkage continue to result in visual loss. This is not amenable to treatment. As a result, elaborate techniques using lateral fields angled 5° posteriorly, patient casts, and anterior electron fields with lead lens shielding have been developed (Abramson et al, 1981). All these methods lacked precision and exact set-up reproducibility, and this may have contributed to the large number of patients receiving at least two courses of external beam radiotherapy (Abramson et al, 1982). Anterior electron fields, even with lens shielding, will contribute a considerable dose to the anterior ocular tissues. In addition, the "penumbra" of the electron fields is

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particularly inferior to that of photons. Thus, a lateral portal could not be employed without considerable scatter through the lens and anterior chamber. To reduce complications further, in suitable patients, Schipper (1980, 1983) developed a lateral field technique using contact lenses and a specially designed applicator. The results of a series of 39 patients were later presented and an excellent cure rate was achieved (Schipper et al, 1985). Eighteen patients developed cataracts, all of whom had part of the posterior aspect of the lens included in the treatment portal.

We have modified the treatment technique devised by Schipper and have sought to verify the stringent dosimetric requirements. Emphasis has been placed on the safe and reproducible immobilisation of the patient, and thus the eye, during the procedure. A report of our technique is presented

## MATERIALS AND METHODS

### *Applicator design and method of treatment*

Treatment is given using a 6 MV Varian linear accelerator, using one or more lateral fields. The treatment-field dimensions and characteristics are defined by a purpose-made applicator mounted in the accessory-tray guides on the head of the treatment unit. The field is D shaped to encompass the posterior segment of the eye and thus the entire retina at risk from this potentially multifocal tumour, and also at least 10 mm of the proximal optic nerve. The dimensions of the major axes of the field are 26 mm × 32 mm at the isocentric distance (100 cm) and it is off-centred from the machine diaphragm rotation axis, such that the anterior beam edge has practically no divergence. The applicator consists of a 41 cm-long aluminium tube centrally mounted on a baseplate. This plate reproducibly locks into the accessory slide of the treatment head. The tube end houses a 12 cm-thick heavy metal insert which collimates the beam (see Fig. 1). Because of its proximity to the patient (typically 13 cm) and the precise, divergent aperture, the collimator gives minimal geometrical penumbra

The patient is immobilised with the aid of a full head shell and anaesthesia. The eye is located by a contact lens with an attached rod which slides in the groove of the contact lens assembly and aligns with a scale (Fig. 1). The rod is magnetically held in the groove. A rigid metal arm is fixed to the applicator and holds the contact lens assembly in its correct position. If bilateral radiotherapy is planned, a second contact lens assembly is placed on the arm, perpendicular to the centre of the contralateral eye (usually 4.5–5.0 cm from the centre of the first assembly). The distance on the scale of the contact lens assembly is set according to the age of the patient. The scale calibration represents the distance between the anterior edge of the radiation beam and the surface of the eye. The final set-up is checked, partly with reference to the light beam and laser lights.

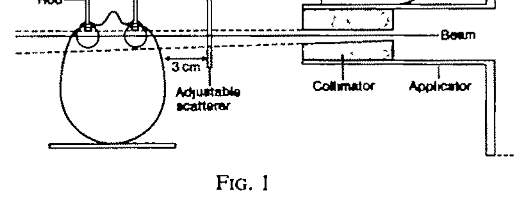

FIG. 1

Diagram of retinoblastoma applicator set up for bilateral orbital irradiation (not to scale)

More anteriorly placed tumours arising from the temporal retina of a young child may lie close to the tissue surface. This is important when considering the build-up characteristics along the beam. A 1 cm perspex screen scatterer has been made which may be placed at varying distances from the skin surface.

### *Dimensions of the eye*

Measurements of the length of the eye, corneal thickness, anterior chamber depth, lens thickness and vitreous length are well documented (Duke-Elder, 1961; Charles & Brown, 1975; Schipper et al, 1985). The change in dimensions with respect to age in children is also known and the individual variation, which is very small, recognised (Francois, 1981). As patients receiving radiotherapy for retinoblastoma are very young, this variation effectively becomes even smaller, and so only one size of applicator (defining the field size) is required The anterior edge of the radiation field should come just behind the posterior pole surface of the lens, the reference point being the surface of the eye. Lens thickness changes little over the first few years of life, and this distance is added to the appropriate anterior chamber depth and corneal thickness. It was thought to be unnecessary to perform individual ultrasound examinations on every patient (unless ophthalmologically deemed necessary).

### *Patient position*

Patient immobilisation is achieved using individually moulded two-section plastic shells. The two halves of the shell lock together on the couch top. Holes are cut in the plastic for the nose, mouth and the eye being treated and over the incident area subtended by the radiation field (Fig. 2).

An adjustable platform has been designed which is placed on the existing automated couch of the linear accelerator. The child lies supine on this platform and the shell is locked into position (Fig. 3). Three large controls allow very fine manual movements in each linear direction. The electrical movements of the existing couch of the linear accelerator are coarse and potentially fast; therefore the manual controls are used for the final set-up in order to achieve greater accuracy under safer conditions. Couch rotation and gantry

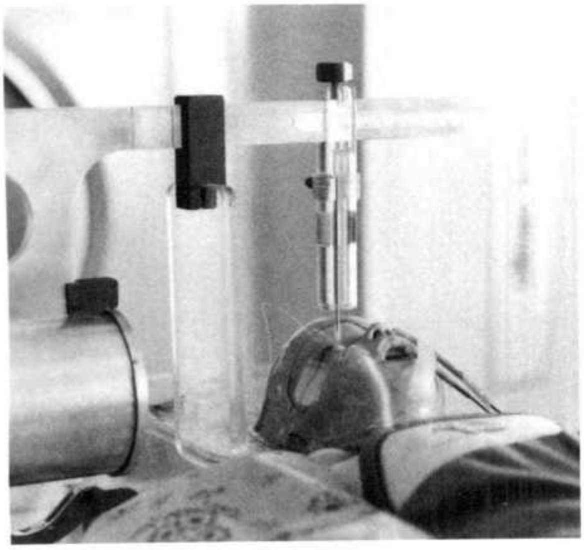

FIG. 2.

Unilateral irradiation. Note the treatment field and laser lights shown, with the child immobilised in the head shell.

angulation are, however, carried out with the electrical control.

*Contact lens and assembly*

Contact lenses have been made by the Ophthalmic Prosthesis Department at Moorfields Eye Hospital specifically for this lateral-beam radiotherapy technique (Fig. 2). They are made of polymethylmethacrylate (PMA) with EN57 steel rods attached to the centre of the convex surface of the lenses. The total length of each contact lens from its inner surface to the end of the rod is manufactured so that it is constant. Three different sizes of contact lens have been designed. Each lens has two curvatures to allow for the different radii of the cornea and conjunctiva. A fine-bore plastic tube is attached to each contact lens. This allows slight suction to be applied if the pupil is not in the centre of the field and also aids in releasing the contact lens at the end of the procedure. Apposition between the eye and contact lens can be seen as the contact lens is transparent. The transparent lens also allows the clinician to check that the eye remains at central gaze. Sterilisation of the contact lens is performed between insertions.

The contact lens assembly locks onto the "arm" of the applicator at the defined position, 15 cm from the end of the collimator (Fig. 2). The rod of the contact lens enters and slides along the groove in the contact-lens assembly. When the end of the rod is aligned with the mid-position of the engraved scale, then the anterior edge of the radiation field will be 8.0 mm behind the surface of the eye. The scale setting may be altered in 0.5 mm intervals from the mid-position; 6.5 mm and 7.0 mm settings on the scale have been used most frequently.

*Dosimetry*

The characteristics of the radiation beam from the applicator have been analysed in three ways.

(1) A small cylindrical ionisation chamber (0.1 $cm^3$, Nuclear Enterprises type 2533/3) was used in a large

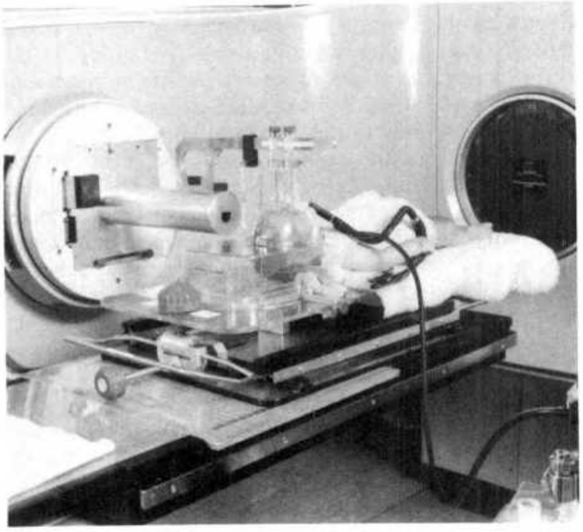

FIG. 3.

Bilateral irradiation showing the child, under general anaesthesia, positioned on the platform ready for treatment.

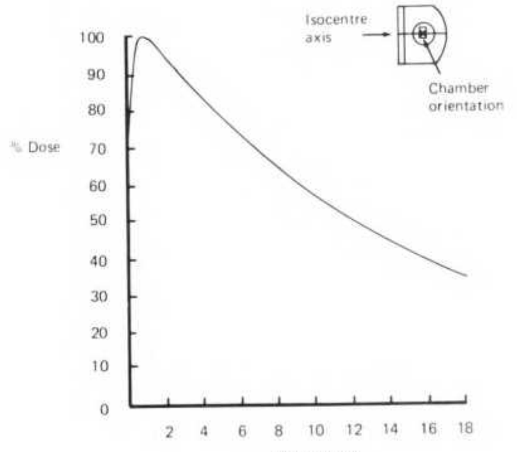

FIG. 4.

Graph showing central-axis depth-dose curve along the 6 MV beam centre obtained using ionisation chambers in a water phantom (skin–source distance (SSD) 97 cm, scatter at 3 cm).

water phantom to obtain the basic central-axis depth-dose curve (Fig. 4). Close to the water surface this technique proved inadequate, because of the chamber geometry, and in this region supplementary integrated dose measurements were taken using a coin-shaped thin-window ionisation chamber (Nuclear Enterprises type 2536). The chamber was built into a variable-geometry solid phantom constructed from a water-substitute plastic resin material, WTI (Constantinou et al, 1982). Inspection of Fig. 4 shows that the build-up effect to 90% was under 0.5 cm and the dose fell to 90% at 3 cm depth. The thin-window chamber was also used to investigate the effect of positioning the 1 cm-thick perspex scatterer at different distances from the phantom surface. For scatterer distances of 1 5, 3.0 and 5.0 cm the 90% isodose is reached at depths of 2.6, 3.75 and 4.6 mm respectively (Fig. 5).

(2) Film dosimetry was used to supplement ionisation-chamber measurements in order to obtain complete spatial dose distributions. Because of their relatively large sensitive volume, ionisation chambers were considered unsuitable for measurements in the rapidly changing field gradients in the penumbra. Envelope-wrapped Kodak RP/V film was exposed in a WTI phantom normal to and parallel to the beam direction, doses of 30 cGy and under were used to remain within the linear characteristics of the film. Densitometry was carried out by scanning the film with a semiautomatic film densitometer (Klevenhagen & Putney, 1974). Figure 6 shows the dose profile obtained from a film (solid line) placed normal to the beam axis at a depth of 3 cm in the phantom. As an illustration, the position of the beam edge relative to a typical 2 cm-diameter eye is also shown and the sharpness of the penumbra, particularly the anterior edge, should be noted. At the back of the lens, at a position corresponding to the projection of the light edge, the dose is just over 50%, yet 3 mm anterior to this, at the front of the lens, it has fallen to less than 10%.

(3) To corroborate the results of the films, detailed dosimetry was also carried out using TLDs on the detachable eye of an anthropomorphic head phantom (Fig. 7A). The phantom manufactured in WTI had been designed with the aim of performing general dosimetry on children's eyes and is strictly representative of a child aged 4–5 years: since all measurements could be related to the position of the surface of the eye it was nevertheless considered a suitable representation for the rather lower age group of interest in this project. One eye of the phantom is constructed to be demonstrable, and an internal cylinder within this eye can be "exploded" and the sections comprising the cylinder interchanged (Fig. 7). Three sections have been precisely constructed to carry TLD chips (Vinten high-sensitivity solid LiF pellets, 4.5 mm diameter, 0.8 mm thick) which can then be positioned, with an accuracy greater than 0.1 mm, at varying depths below the anterior surface of the eye. The dose profile obtained from TLD measurements made in the region of the lens is shown by the dotted line in Fig. 6. The reproducibility of the TLD system is within 1.7% (two standard deviations). While demonstrating excellent positional agreement with the film measurements, the results suggest an even sharper penumbra than is indicated by the film, reflecting perhaps the better measurement resolution of the chips, from their smaller physical size in the direction of profile (0.8 mm compared with the densitometer aperture of 1.0 mm).

The phantom was also used to investigate whether

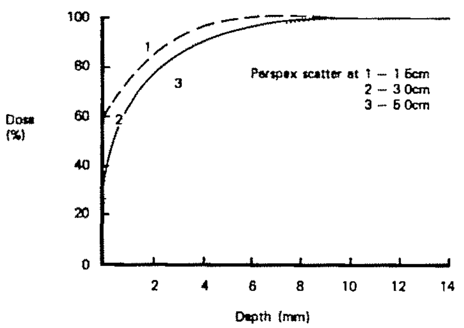

FIG. 5.

Dose build-up characteristics along the beam centre with the perspex scatterer at 1.5 cm, 3.0 cm and 5 0 cm from the tissue surface (SSD 97 cm).

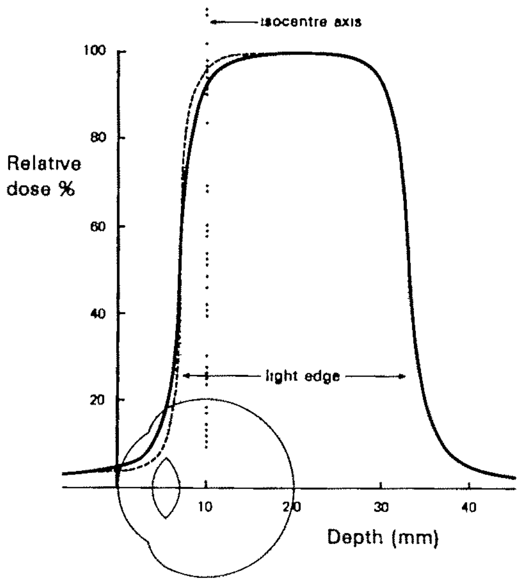

FIG. 6

Dose profile at 3 cm depth (SSD 97 cm) readings obtained from scanning-densitometer (——) and thermoluminescent dosemeters (TLDs) in the phantom (– – – –). A diagrammatic representation of the child's eye is shown.

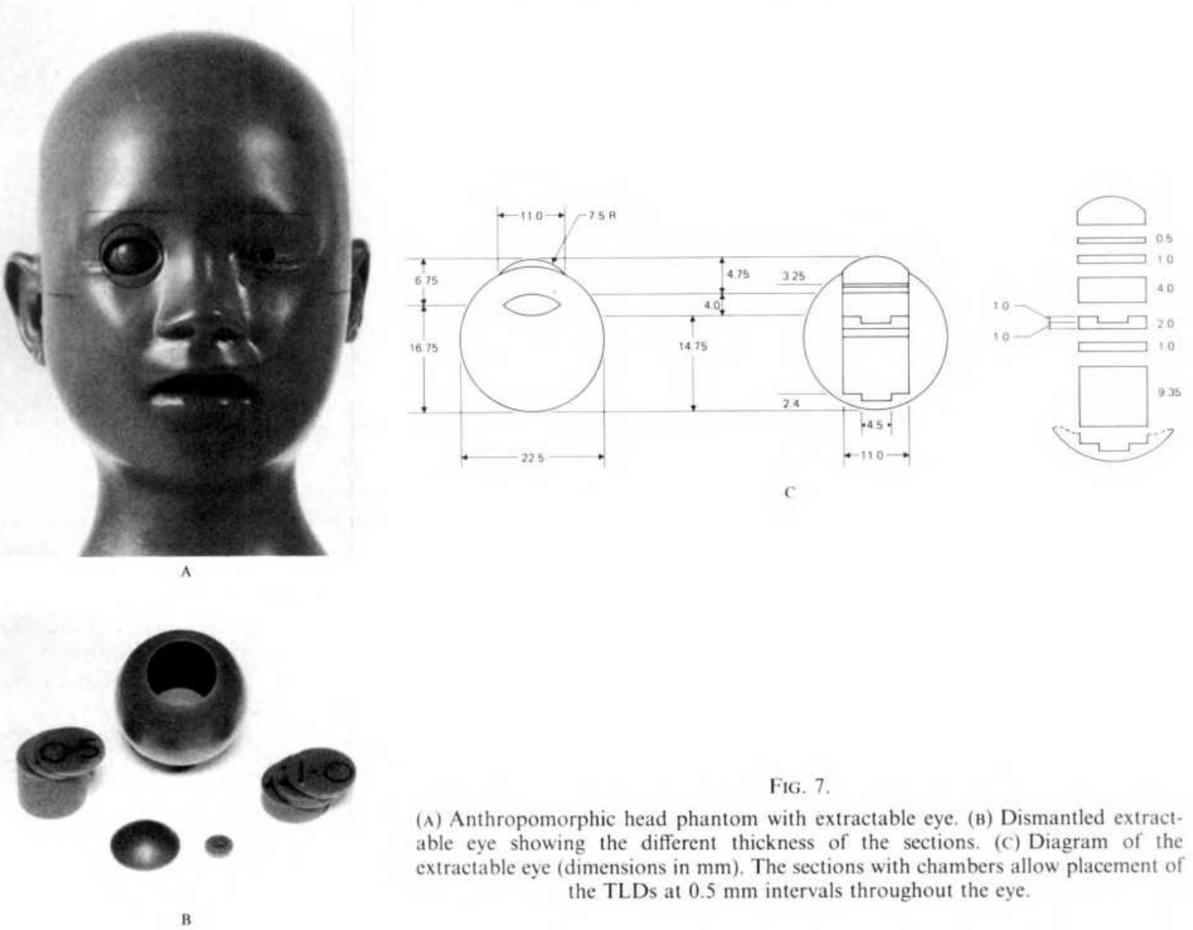

FIG. 7.

(A) Anthropomorphic head phantom with extractable eye. (B) Dismantled extractable eye showing the different thickness of the sections. (C) Diagram of the extractable eye (dimensions in mm). The sections with chambers allow placement of the TLDs at 0.5 mm intervals throughout the eye.

different positions of the perspex scatterer had an influence on the dose received by the lens. No significant change in lens dose was detected with the scatterer at distances varying from 2 mm to 92 mm from the tissue surface. It has, therefore, been established that the perspex scatterer improves the retinal dosimetry and in no way interferes with the sharpness of the beam edge anteriorly.

Whilst considering dosimetry, there are three different treatment situations, which are discussed below.

(1) After enucleation of the contralateral eye has been performed, unilateral irradiation with a direct lateral field is used, as the radiation beam will not then exit through a normal eye (Fig. 2).

(2) Bilateral irradiation is recommended for suitable tumours involving both eyes. Two contact lenses and assemblies are employed and the ends of both rods aligned with each scale. The "first" eye is set up at the isocentre, correctly positioned and treated. Adjustments, when necessary, are made to the gantry and couch angles so that the contralateral eye is in the correct position (Fig. 3). The second lateral field is similarly set up and treated. The dose is prescribed to the midline.

(3) When unilateral irradiation is required and the contralateral eye excluded from the path of the radiation portal, the couch has to be rotated after the involved eye has been set up at the isocentre. To find the angle of rotation required, measurements were again made on the anthropomorphic head phantom. Thermoluminescent dosemeters were placed at two levels through the centre of the contralateral eye, and at a position on the circumference between 7 and 8 o'clock, at a depth of 1.25 cm (Fig. 7A). Measurements were taken with the couch at varying angles (see Fig. 8). To achieve an acceptable level of dose (less than 5%) to the periphery of the contralateral eye, it is necessary to rotate the couch 40° to the beam axis. As the ipsilateral eye axis is coincident with the machine isocentre no "geometric miss" of the eye will occur with couch rotation.

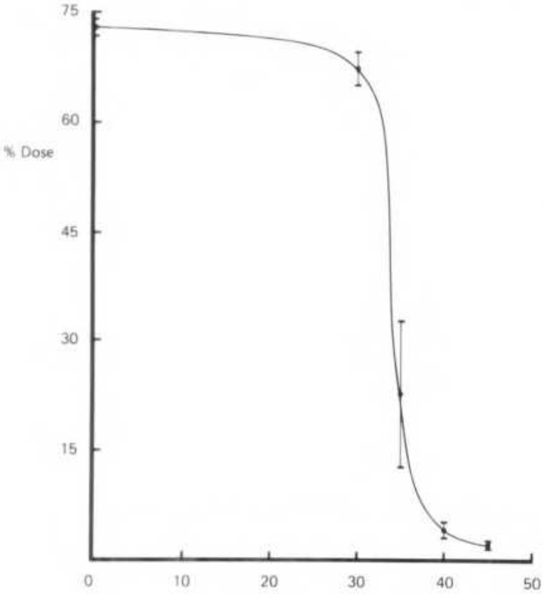

FIG. 8.

Percentage dose received at the circumference position in the contralateral eye against the angulation of the field.

*Scale calibration check*

The dosimetry has shown that it is possible to achieve a small radiation field which is sharply defined and non-divergent anteriorly. The dose to the anterior chamber and lens of the eye is therefore minimal. This is of little value if the anterior beam edge is not at the correct level through the eye(s) to within an accuracy of within 0.5 mm. A description of the method used for checking the calibration follows.

The removable eye of the phantom is employed; it has an anterior–posterior diameter of 23.5 mm. It is placed on a lead block on the treatment couch. The contact lens is placed on the eye and aligned to the 8 mm mark on the scale. A film is placed behind the eye phantom and exposed, thus simulating a patient set-up. The development film shows the radiation field and the back of the eye demarcated by the lead block. This distance from the anterior field border to the back of the eye is 15.5 mm, confirming the 8.0 mm setting on the scale. This test is undertaken regularly to cross-check the reproducibility of the method.

*Radiotherapy dose prescription*

The dose employed is 4000 cGy prescribed at depth and given in 20 fractions over 30 days. The daily applied dose in this situation is approximately 220 cGy for treatment of a unilateral eye.

*Field verification*

The described technique must achieve positional accuracy not likely to be reached in other areas of radiotherapy. Conventional simulation of the treatment field has proved unhelpful; however, a double-exposure port film on the therapy machine provides good verification of beam alignment. For this procedure the applicator assembly is carefully removed and the field size increased before the second exposure is taken. The dose of 2 cGy to this large area is acceptable. A radiograph is thus produced which defines both the radiation portal and the detailed outline of the child in the treatment position. The front of the eye can be clearly seen, but lead markers can be added if necessary (Fig. 9).

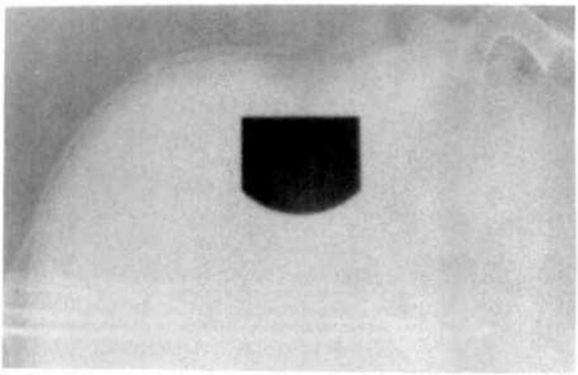

FIG. 9.

Check beam film obtained of treatment portal.

*Anaesthetic details*

The above dose prescription requires daily treatment; to achieve complete immobilisation of very young children, an anaesthetic is required. Repeated general anaesthesia is attended by its own problems and possible complications. Daily intubation was considered too hazardous. A technique of giving anaesthesia via a Portex airway with a Cobb's connector inserted into the airway connected to an air T piece alleviated the need to intubate the baby (Fig. 3). Continuous respiratory and pulse sensor thermistors were used throughout treatment (Fig. 2). This has now been replaced by continuous electrocardiogram monitoring.

A pre-medication is used of hyoscine 0.08 mg/kg or atropine 0.015 mg/kg and, if the child is over 1 year old, Vallergan (May & Baker) 3–4 mg/kg is also given. The general anaesthetic of a mixture of nitrous oxide and oxygen and 2% halothane follows at the normal period after the pre-medication. The plane of anaesthesia is below that which is associated with Bell's ocular phenomenon. When the contact lens has been inserted and the radiation field set up appropriately, the anaesthetic is continued during treatment. The monitors, Ambu bag, and respiratory movements of the chest are all viewed by closed-circuit television throughout the radiation treatment, which lasts about 1 min. The nitrous oxide and 2% halothane are then discontinued and the patient recovers in about 15 min and is then observed on the ward until fully awake. With this procedure, many patients have been managed as outpatients and none have required daily intubation. On many occasions, ketamine anaesthesia has been found to be sufficient for the required immobilisation in the full head shell.

## DISCUSSION

Where external beam radiotherapy is appropriate for treatment of retinoblastoma, it has been traditional to employ whole-eye radiotherapy. Previous techniques of lateral beam therapy were crude, until Schipper (1980) devised an accurate method of beam-edge positioning using a contact lens as a reference point; subsequent clinical reports of this technique have been published (Schipper, 1983, Schipper et al, 1985). We have adapted the basic Schipper technique and in doing so incorporated our extensive local experience of treating this disease. Areas of particular concern included fractionation and dose, positioning and immobilisation of the patient and precise dosimetry.

With regard to the total dose delivered, it is not our policy to deliver a dose greater than 4000 cGy in 20 fractions by this new technique (although massive tumours receiving whole-eye radiotherapy receive 4400 cGy in 22 fractions). The dose regimens of 3600 cGy in 12 fractions at three per week (1392 rets) previously, or 4000 cGy in 20 fractions at five per week (1368 rets) currently, have been studied at these hospitals for some years and Bedford et al (1971) have reported results from such treatments that do not justify a higher dosage. We expect that this lower total dosage and the lower daily dose fraction size in the current dose prescription will further reduce late morbidity in the follow-up of the cohort of patients being studied after treatment with this new technique. Indeed, in an unpublished review of our patients with retinoblastoma treated by radical whole-eye external beam radiotherapy of 3600 cGy in nine or 12 fractions or of 4000 cGy in 20 fractions, the late morbidity is reduced in the 20-fraction group. This has implications for techniques which employ general anaesthesia by intubation and therefore do not treat the patients daily. In London, the patients receive general anaesthesia safely without intubation.

In addition, it was considered that even small degrees of head rotation would vitiate the objectives of the technique and that a full head shell was necessary. In consultation with our anaesthetic colleagues, anaesthesia is now safely executed and monitored in the fully shelled, anaesthetised, supine infant.

The next concern that arose was with the safety of using automated, remote couch controls to manoeuvre the fixed, supine infant with the rod-connected contact-lens apparatus *in situ*. A manually controlled platform is used for the final adjustments in bringing the child's eye up to the exact treatment distance. The beam-profile characteristics were cross-checked by at least two independent methods, including one method in an exact anthropomorphic phantom of a child's head. Both methods described here show excellent positioning agreement The calibration of the scale and contact-lens assembly should be checked. We developed a simple and direct method using the removable eye of the phantom and film. In addition, the accuracy of the field with the child in the treatment position was again checked by a simple method which allowed detail to be seen and thus allowed confirmation to be made.

The double check on the calibration of the contact-lens assembly and the anterior beam edge dose profile are both highly critical for unilateral and parallel opposed, bilateral ocular radiotherapy. The clinical accuracy of this technique depends upon the placement of the anterior beam edge. Posteriorly, a minimum length of 10 mm of the optic nerve will always be included in the field. For unilateral ocular radiotherapy, with the contralateral eye *in situ*, the angle of approach must be altered to avoid the contralateral eye. However, it is undesirable to exit the radiation beam through the contralateral frontal lobe of the brain (or indeed to enter through the ipsilateral lower face). The angle of approach is therefore superior rather than inferior. The lateral beam edge is not as sharp as the anterior beam owing to some divergence of the radiation beam. This should be considered, as it will tend to increase the dose to the contralateral eye. The data presented show that, at an angle of 40°, the periphery of the contralateral eye receives a negligible dose of 4% of the radiotherapy prescription, but with a lower angle the dosage rises sharply.

If the angle is above 40°, then a larger volume of the contralateral lower facial tissues and indeed part of the ipsilateral frontal lobe would be in the path of the radiation beam. At 40° the ipsilateral frontal lobe is practically excluded from the beam and the volume to the contralateral maxilla will be minimised. The percentage dose this latter area receives from the small field size of 26 mm × 32 mm in a sagittal plane below the centre of the contralateral eye will have fallen to approximately 60%, 2400 cGy for a prescription of 4000 cGy (see Fig. 4). Thus morbidity is minimised.

In conclusion, a standard 6 MV linear accelerator beam has been modified to produce a non-divergent and almost penumbra-free beam edge and this edge placed with a 0.5 mm accuracy behind the front surface of a supine, immobilised and anaesthetised infant's eye in order to produce a significant advance in the treatment of retinoblastoma by external beam radiotherapy. Considerations that led to the development of the original Dutch technique and the results of experimental studies have been presented.

## ACKOWLEDGMENTS

We are grateful for the assistance and co-operation of our anaesthetic colleagues and radiographers, and Dr S. C. Klevenhagen for the use of the scanning densitometer. We thank Miss T Cocks and Miss C. Simmons for typing the manuscript and the Medical Illustration Department of St

Bartholomew's Hospital for the preparation of the diagrams. We thank Mr D. Doughty for advice and for checking the manuscript.

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# Quantitative magnetic resonance imaging in rectal carcinoma

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(*Received September 1986 and in revised form November 1986*)

## ABSTRACT

$T_1$ and $T_2$ relaxation times have been calculated in 30 patients with rectal carcinoma and seven patients with a fibrotic pelvic mass. The relaxation times were calculated using a multipoint iterative method with data from seven total saturation recovery and six spin-echo sequences. The results show that the calculated $T_1$ relaxation value is a useful discriminant between carcinoma and pelvic fibrosis and should improve the detection of early tumour recurrence.

X-ray computed tomography (CT) is the optimal method for confirming tumour recurrence in patients who have had primary surgery for carcinoma of the rectum, especially if an abdomino-perineal (AP) resection has been undertaken (Husband et al, 1980; Lee et al, 1981; Zheng et al, 1984). However, most patients are diagnosed when they are symptomatic, for example, having pelvic pain or rectal discharge, and at such time treatment is usually palliative. Earlier detection, with improved survival, might be possible if patients had repeated CT scans at suitable intervals after surgery, although to adopt this policy for all patients would be logistically difficult in most UK health regions.

Even in symptomatic patients, there are problems in CT scan interpretation which cannot be overcome by improvements in technique. These relate to the inability of CT to characterise tissue and, when an isolated pre-sacral mass is seen, to distinguish between tumour or post-operative fibrosis (Fig. 1). In this situation, a percutaneous needle aspiration biopsy or second-look laparotomy is required to obtain tissue for histology. A negative percutaneous biopsy is unreliable in the exclusion of tumour. A negative biopsy obtained at surgery is more reliable, but the patient will have been submitted to potentially hazardous surgery. The problem of differentiation between post-operative fibrosis and early tumour recurrence is likely to be encountered more frequently on routine scanning of asymptomatic patients.

Magnetic resonance imaging (MRI) has the potential to characterise tissue and therefore, perhaps, to distinguish between fibrosis and tumour. In Manchester we have approached the task of tissue characterisation by measuring $T_1$ and $T_2$ relaxation times, using a multipoint iterative analysis (Hickey et al, 1986b; Isherwood et al, 1986) which, in a series of clinical and experimental studies (Jenkins et al, 1985a, b, 1987), has proved to be both robust and reproducible. This paper reports the results from using the method in an attempt to distinguish between post-operative fibrosis and recurrent rectal carcinoma and thereby improve the detection of early tumour recurrence.

## MATERIALS AND METHODS

Thirty-seven patients (27 men, 10 women, age range 38–81 years) were examined. There were 28 patients with biopsy-proven locally recurrent adenocarcinoma of the rectum, two patients with biopsy-proven new carcinoma of the rectum and seven patients with a fibrotic pelvic mass. These last seven patients had had previous surgery and were selected on the basis of the presence of a pre-sacral mass which had not changed in size or appearance on CT scans for a minimum of 2 years. All patients with new or recurrent carcinoma of the rectum were selected for study after a CT scan had demonstrated the presence of a tumour greater than 5 cm in one diameter. These patients then had an MR scan within 7 days (Fig. 2).

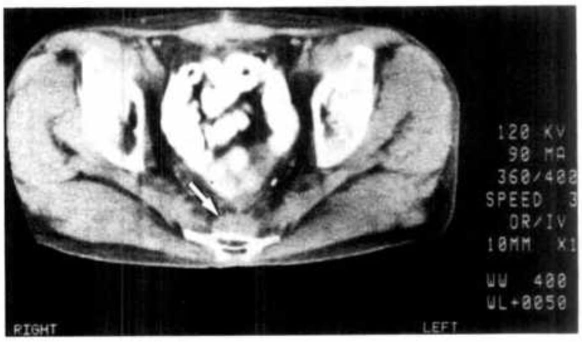

FIG. 1.

Pelvic CT scan. In an asymptomatic patient the pre-sacral soft-tissue mass (arrowed) could represent recurrent tumour or fibrosis. This was tumour recurrence after AP resection.

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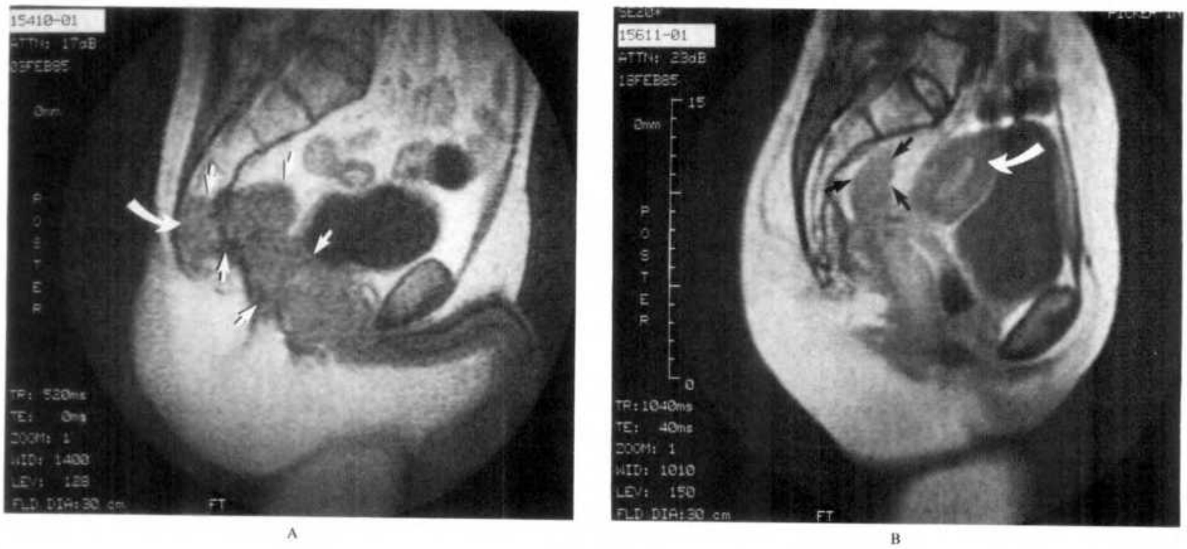

A

B

FIG. 2.

Sagittal MR images demonstrating recurrent rectal carcinoma (straight arrows) in two patients. (A) $T_1$-weighted image (TSR 350) with infiltration of lower sacrum (curved arrow), bladder and prostate. (B) Intermediate weighted image (SE 1040/40) with bulk disease separate from the uterus (curved arrow) and sacrum.

All MR images were obtained on a Picker International superconducting magnet system operating at 0.26 T and using a two-dimensional Fourier transform (2DFT) reconstruction. To calculate the $T_1$ and $T_2$ relaxation times, initial siting scans were performed in three orthogonal planes to identify the optimal site for data collection from the tumour or fibrotic mass. All data were collected in the sagittal plane, using a 30 cm field of view and 1 cm-thick sections. Data within a region of interest from seven total-saturation recovery (TSR) (Waterton et al, 1984) and six spin-echo (SE) sequences were used to calculate the $T_1$ and $T_2$ relaxation times by an iterative least-squares method (Hickey et al, 1986b). The corresponding Pearson correlation coefficients (Beaumont, 1972) obtained for $T_1$ and $T_2$ were $> 0.92$ for all results; the majority had values $> 0.99$. Approximately 50 min per patient was needed to collect the 13 MR data images using 64 gradient increments, each with two signal excitations. The measured values from patients with tumour and patients with a fibrotic mass were compared using Student's *t*-tests.

After quantitative data had been collected, multisection images were obtained in the sagittal and coronal plane using $T_1$- and $T_2$-weighted sequences in order to assess the size and extent of tumour. These images are currently being analysed in a CT/MR correlative study and will be reported separately.

## RESULTS

The mean $T_1$ and $T_2$ relaxation times of 30 patients with carcinoma of the rectum and seven patients with a fibrotic mass are presented in Table I. Individual $T_1$ and $T_2$ values are detailed in Figs 3 and 4 respectively. The $T_1$ values plotted against the $T_2$ values for all 37 patients are given in Fig. 5.

The results demonstrate a highly significant difference ($p < 0.001$) between the mean $T_1$ values for carcinoma of the rectum and fibrosis. There is, however, no significant difference in the $T_2$ values. Figure 3 reveals that two of the patients with a fibrotic mass had $T_1$ values within the lower range of values for carcinoma of the rectum. Figure 4 demonstrates the considerable overlap of $T_2$ values from the two conditions. Separation of the two groups was not improved by plotting $T_1$ against $T_2$ values (Fig. 5).

## DISCUSSION

The problems of differentiating between post-operative fibrosis and early tumour recurrence on a CT scan, and the difficulties this can cause in clinical management, are well recognised. We have attempted

TABLE I

CARCINOMA OF THE RECTUM AND FIBROSIS: MEAN RELAXATION TIMES ± SE

| | $n$ | $T_1$ (ms) | $T_2$ (ms) |
|---|---|---|---|
| Carcinoma of the rectum | 30 | $817 \pm 29$* | $69 \pm 3$ |
| Fibrosis | 7 | $458 \pm 67$* | $58 \pm 3$ |

*Highly significant difference ($p < 0.001$).

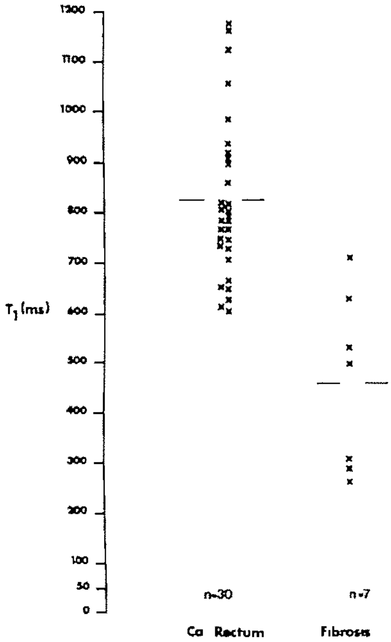

FIG 3

Histogram showing the distribution of $T_1$ relaxation times for 30 patients with carcinoma of the rectum and seven patients with pelvic fibrosis The horizontal bar represents the mean $T_1$ value

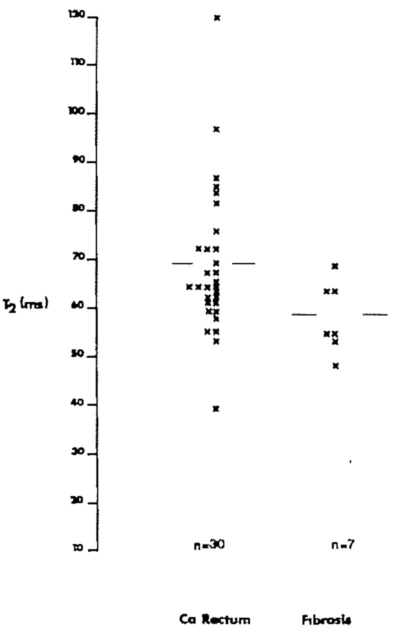

FIG 4

Histogram showing the distribution of $T_2$ relaxation times for 30 patients with carcinoma of the rectum and seven patients with pelvic fibrosis. The horizontal bar represents the mean $T_2$ value.

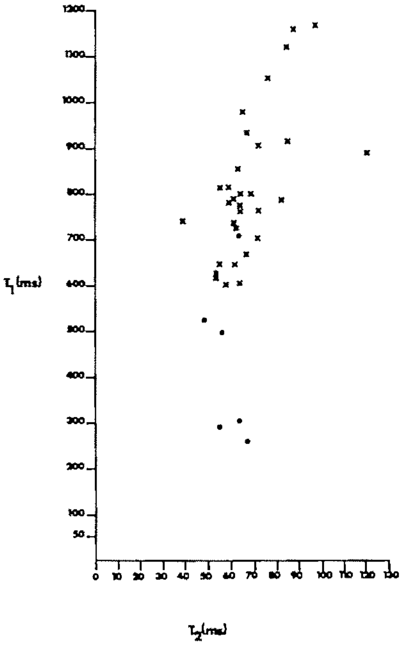

FIG. 5.

Individual $T_1$ and $T_2$ relaxation times for 30 patients with carcinoma of the rectum (X) plotted against the individual $T_1$ and $T_2$ relaxation times for seven patients with pelvic fibrosis (●)

to distinguish the two conditions by a quantitative approach measuring $T_1$ and $T_2$ relaxation times. The method, which employs a multiple data point approach and a slice profile independent of the pulse repetition time (TR), was designed to eliminate some of the technical errors (Hickey et al, 1986b; Isherwood et al, 1986). The results from this study suggest that the measured $T_1$ relaxation time is a reliable discriminant between rectal carcinoma and fibrosis in the majority of cases and, in this series, universally when $T_1$ was longer than 725 ms. The measured $T_2$ relaxation times were of no value in differentiation.

The number of patients in the fibrotic group is small and the statistical limitations imposed by the size of the group are recognised. There are, however, real difficulties in obtaining patients with a proven pelvic fibrotic mass which has remained unchanged in size and appearance over several years, and who are willing to undergo quantitative MR studies. This is the first study, nevertheless, to document a quantitative difference between tumour and fibrosis, albeit with overlap in two patients. To explain the observed differences, the physical state of water must be considered. The fast proton diffusion model (Fullerton et al, 1982) suggests that the $T_1$ relaxation parameter is dominated by two factors: the total water content, and the ability of tissue macromolecules, viz. proteins and nucleic acids, to bind water in the hydration layer. Bound water is restricted in its molecular motion. The observed relaxation time is a weighted average of this quickly relaxing bound fraction and the more slowly relaxing bulk water (Bakker & Vriend, 1983). The longer $T_1$ values of tumour compared with fibrosis are therefore probably related to a greater total water content and the fact that less of the water is bound to macromolecules.

The measured $T_1$ and $T_2$ relaxation times have been calculated from a region of interest on one image, taken through one area of the tumour or fibrotic mass, and we recognise that these values may vary from region to region within the mass, particularly since tumour and fibrosis may be mixed. The time taken, however, to collect the data for $T_1$ and $T_2$ measurement (50 min) does not allow for more than one section within the tumour to be sampled Pixel distribution of calculated $T_1$ and $T_2$ values in the form of tissue maps and their subsequent textural analysis may provide more information than regions of interest (Conners & Harlow, 1980; Hickey et al, 1986a; Isherwood et al, 1987). Such an approach is currently being used to obtain further baseline data, and will be used in a longitudinal study comparing these data with second-look laparotomy in those patients suspected of tumour recurrence (Johnson et al, 1986).

## Conclusion

Preliminary data from the measurement of $T_1$ and $T_2$ relaxation times in patients with rectal carcinoma and pelvic fibrosis demonstrate that the calculated $T_1$ relaxation value is a useful discriminant. Such a measurement should improve the detection of early tumour recurrence.

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1987, *The British Journal of Radiology*, 60, 765–770 AUGUST 1987

# Radiological features of systemic mast-cell disease

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(*Received October 1986*)

ABSTRACT

Radiological studies were done on 23 patients with systemic mast-cell disease (SMCD). Significant changes occur most often in bones and less commonly in the gastrointestinal tract and other visceral organs. These changes may be related either to tissue infiltration by mast cells, or to the effect exerted on tissues by chemical mediators of the mast cells, although in some instances findings may be coincidental Because the radiological changes are not unique to SMCD, their main value, in association with the clinical information, is in directing further studies for diagnostic confirmation and in estimating the extent of systemic involvement.

In 1877, Paul Ehrlich studied in the connective tissues a type of cell with highly refractile granules in his polychrome staining method. He found that these cells possessed a specific affinity for basic dyes and that they were stained purple (metachromasia) with aniline dyes such as toluidine blue. He called these cells "Mastzellen", or mast cells. These cells are found most often in connective tissue around the vessels and beneath the capsular tissues of most organs; human lung is extremely rich in mast cells. Their origin is still controversial, but recent evidence seems to support the theory that they are derived from haemopoietic stem cells (Denburg et al, 1983), their fate is unknown. Mast cells contain a vast number of chemical mediators, including heparin, histamine and serotonin (Lewis & Austen, 1977) and are capable of responding to neural, chemical and immunological stimulations by releasing these mediators which, when excessive, may cause signs and symptoms such as broncho-constriction, oedema and anaphylaxis. Mast cells are heterogeneous and can be subclassified, according to their cellular composition and tissue distribution, into mucosal and connective-tissue subtypes (Katz et al, 1985).

Uncontrolled growth of mast cells in tissue is an uncommon disorder which can be categorised into urticaria pigmentosa, mastocytoma, systemic mast-cell disease (SMCD) and mast-cell leukaemia (Sagher & Even-Pat, 1967; Lennert & Parwaresch, 1979). Urticaria pigmentosa is the most common mast-cell disease, accounting for 80–90% of the mastocytosis. It presents mainly as pigmented skin lesions and occurs most often in young children, tending to regress in adolescence. Cases which do not regress progress into SMCD Mastocytoma is an extremely rare form of the disease, manifesting as isolated skin nodules, and its natural course is unknown. Mast-cell leukaemia is also very rare and is characterised by mast-cell involvement of blood, bone marrow and other organs. It usually presents with signs and symptoms of acute leukaemia, responds poorly to chemotherapy and has a brief clinical course.

Systemic mast-cell disease is another rare form of mastocytosis and is characterised by mast-cell involvement in many organs, except the peripheral blood. Individual case reports dominate the literature and its natural history remains uncertain. Skin lesions characteristic of urticaria pigmentosa may be seen in only 50% of cases (Webb et al, 1982). In those cases without skin lesions, the presenting features may be too non-specific to indicate SMCD and any clinical and laboratory studies that help to arouse clinical suspicion of SMCD are welcome. Although the diagnosis of SMCD rests finally on identification of mast cells by histopathological examination of the involved tissues, radiological studies may suggest more decisive tests.

The radiological findings in bone, lung, gastrointestinal tract and lymph nodes were described sporadically in several small series of cases (Szweda et al, 1962; Bank & Marks, 1963; Clemett et al, 1968; Dantzig, 1975; Ammann et al, 1976; Cryer & Kissane, 1976; Feldman & Isenberg, 1976; Fishman et al, 1979; Lucaya et al, 1979). These have been summarised by Sagher and Even-Pat (1967). The lymphographic findings have also been reported (Hancock et al, 1976; Tubiana et al, 1979) In this paper, we describe the radiological findings in 23 patients with SMCD and examine the diagnostic value of computed tomography, sonography and radionuclide studies.

## MATERIAL AND METHOD

The records were examined of all cases of SMCD in the files of two of the authors (L.T.Y. and C.Y.L.). Twenty-three cases with adequate clinical information and radiological studies are included The clinical and histopathological findings in 20 of these 23 patients have been reported previously (Webb et al, 1982). In each patient, the clinical features, including the age, sex,

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TABLE I

CLINICAL FINDINGS IN 23 PATIENTS

| Case No. | Age (years) | Sex | Chief problems | Initial diagnosis | Duration (years: months) | Outcome |
|---|---|---|---|---|---|---|
| 1 | 49 | F | Heartburn, skin lesion | Peptic ulcer disease | 12 | Alive |
| 2 | 78 | F | Fever, anaemia, | Lymphoma | 2 | Died: gastrointestinal bleeding |
| 3 | 76 | F | Skin lesion, adenopathy | Urticaria pigmentosa | 13: 7 | Died: sarcoma |
| 4 | 60 | F | Skin lesion, diarrhoea | Carcinomatosis | 9: 5 | Died: mesothelioma |
| 5 | 40 | F | Skin lesion, flushing | Urticaria pigmentosa | 8: 7 | Died: histamine shock |
| 6 | 67 | F | Skin lesion, diarrhoea | Peptic ulcer disease | 14: 3 | Alive |
| 7 | 57 | F | Skin lesion, flushing | Urticaria pigmentosa | 7: 11 | Alive |
| 8 | 69 | F | Fatigue, dysuria | Thrombocytosis | 6: 9 | Alive |
| 9 | 60 | F | Back pain, dyspnoea | Lumbar-disc syndrome | 8 | Alive |
| 10 | 65 | F | Fatigue, arthralgia | Hypertension | 11 | Alive |
| 11 | 48 | F | Skin lesion, anaemia | Unknown fever | 2: 3 | Alive |
| 12 | 72 | F | Ascites | Lymphoma | 1: 8 | Died: SMCD |
| 13 | 62 | F | Epigastric pain | Cholecystitis | 0: 2 | Died: SMCD |
| 14 | 38 | M | Diarrhoea, flushing | Carcinoid syndrome | 0: 1 | Died: histamine shock |
| 15 | 52 | M | Skin lesion, anaemia | Myelofibrosis | 2: 4 | Died: SMCD |
| 16 | 63 | M | Fever, diarrhoea | Cholecystitis | 4: 6 | Died: respiratory failure |
| 17 | 58 | M | Fatigue, weakness | Carcinomatosis | 0: 5 | Died: pancreatic cancer |
| 18 | 34 | M | Flushing, weight loss | Carcinoid syndrome | 21 | Alive |
| 19 | 32 | M | Skin lesion, back pain | Fracture of T12 | 8 | Alive |
| 20 | 62 | M | Skin lesion, diarrhoea | Urticaria pigmentosa | 8 | Alive |
| 21 | 50 | M | Skin lesion, pruritus | Urticaria pigmentosa | 4: 8 | Alive |
| 22 | 68 | M | Flushing, heartburn | Peptic ulcer disease | 2: 6 | Died: chronic myeloid leukaemia |
| 23 | 79 | M | Diarrhoea, syncope | Hepatomegaly | 3 | Alive |

presenting symptoms, physical findings and laboratory studies, were reviewed (Table I) and all available radiological studies were examined (Table II). For cases in which the original studies were not available, the reports issued by the original examiners were used. These radiological studies were usually derived under one or more of the four following circumstances: incidental findings at routine examination; evaluation of specific complaints such as low back pain, "menopause syndrome" with skin flushing, osteoporosis and skeletal fracture; gastrointestinal signs and symptoms; and occult neoplasms or infections.

## RESULTS

### *Chest*

Findings included fibrosis throughout both lung fields and the hilar regions in 10 patients. Cardiomegaly was noted in five patients, pleural effusion in two and pulmonary oedema in one.

### *Skeletal system*

Skeletal changes occurred in 69% of cases. Osteoblastic lesions were present in eight, pure osteolytic lesions in one, and mixed osteoblastic and osteolytic lesions in seven (Fig. 1). Although any anatomical site may be affected, the skull, vertebral column, ribs and pelvis tend to be involved most frequently. One patient had a pathological fracture of the left inferior pubic ramus and three patients had vertebral compression fractures. Two of these 16 patients had bone involvement only. In five patients, the radiographic findings were normal, although marrow biopsies revealed definite involvement by mast cells. Only two

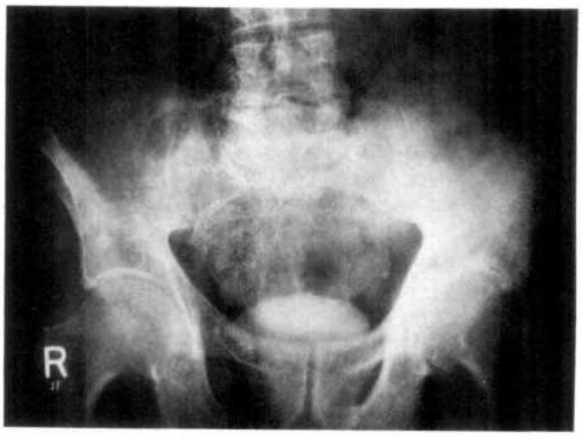

FIG. 1.

Pelvis showing mixed osteoblastic and osteolytic lesions in SMCD.

TABLE II

RADIOLOGICAL MANIFESTATIONS OF SMCD

| Radiological changes (No of patients studied) | Abnormal findings | |
|---|---|---|
| | No of patients | % |
| Chest (23) | 18 | 78 |
| Interstitial fibrosis | 10 | |
| Pleural effusion | 2 | |
| Pulmonary oedema | 1 | |
| Cardiomegaly | 5 | |
| Bone (23) | 16 | 69 |
| Osteoblastic lesions | 8 | |
| Osteolytic lesions | 1 | |
| Mixed blastic and lytic lesions | 7 | |
| Oesophagus (21) | 6 | 28 |
| Hiatus hernia/oesophagitis | 2 | |
| Hiatus hernia/reflux | 3 | |
| Motor inco-ordination | 1 | |
| Stomach (21) | 6 | 30 |
| Gastric nodules | 4 | |
| Gastritis/ulcer | 2 | |
| Duodenum (21) | 12 | 57 |
| Duodenal nodules | 3 | |
| Duodenitis | 2 | |
| Acute or chronic ulcer | 7 | |
| Small bowel (14) | 4 | 29 |
| Jejunal or ileal nodules | 2 | |
| Sluggishness, dilatation, segmentation | 2 | |
| Colon (15) | 6 | 40 |
| Colonic nodules | 1 | |
| Diverticulosis | 5 | |
| Gallbladder (9) | 5 | 56 |
| Non-functioning organ | 2 | |
| Gallstone | 3 | |
| Liver (21*) | | |
| Hepatomegaly | 6 | 28 |
| Spleen (21*) | | |
| Splenomegaly | 4 | 20 |
| Lymph node (abdominal CT, 5) | | |
| Retroperitoneal adenopathy | 3 | 60 |

*Including abdominal radiographic studies in 20, liver and spleen scanning in eight and abdominal computed tomography in five patients.

patients showed no bony abnormality by either radiological or histological studies.

### *Gastrointestinal tract*

Upper gastrointestinal studies revealed significant findings in 14 patients. Oesophageal abnormalities included hiatus hernia in five, oesophagitis in two, and motor inco-ordination in one patient. Findings in the stomach included polypoid nodulation in four patients (Fig. 2) and two showed gastritis and ulcerations; duodenal ulcers were found in seven patients, nodulations in three and duodenitis in two.

Small-bowel studies in 14 patients showed nodulation of the ileum in two and malabsorption patterns in two.

Barium enemas were performed in 15 patients, but only one had definite involvement of the colon, showing multiple nodules in the caecum, ascending colon and transverse colon. Five showed diverticulosis which may have been coincidental. Cholecystographic studies in nine patients revealed two with a non-functioning gallbladder and a contracted gallbladder with a thick wall was found on sonography in one patient (Fig. 3A). The gallbladder wall of this patient was found to have extensive mast-cell infiltration (Fig. 3B). Three patients had gallstones.

### *Radionuclide studies*

Liver and spleen scans were done on eight patients and revealed diffuse hepatomegaly in six and splenomegaly in four (Fig. 4). Histological studies made on liver tissues in four patients and on the spleen in four patients all confirmed mast-cell infiltration. Bone scans were done on four patients. Three showed no significant changes but one exhibited diffuse increased uptake, especially in the proximal extremities.

### *Computed tomography*

Computed tomography of the head was performed in three patients because of pressure symptoms but no abnormality was noted. Abdominal scans were performed on five patients initially suspected of having occult malignancy in the abdomen. Of these, three were found to have generalised enlargement of the retroperitoneal lymph nodes (Fig. 5), one had hepatosplenomegaly, three had hepatomegaly and one had splenomegaly

### *Genito-urinary tract*

Intravenous pyelography performed on five patients was normal in each case and no genito-urinary tract involvement was demonstrated in other radiological studies, including radionuclide scanning and abdominal computed tomography.

## DISCUSSION

The diagnosis of SMCD was established in the patients in our series by histopathological demonstrations of involved tissues. The initial clinical manifestations in these patients, however, were non-specific and variable, requiring extensive examinations to establish the diagnosis. The radiological studies included in this report were performed as part of these diagnostic tests.

Radiological changes occur frequently in mastocytosis; bone changes are the most commonly reported, occurring in 70% of cases (Sagher & Even-Pat, 1967). The bones may show osteoporotic, osteosclerotic or mixed changes which may be either diffuse or circumscribed. The diffuse lesions are often poorly

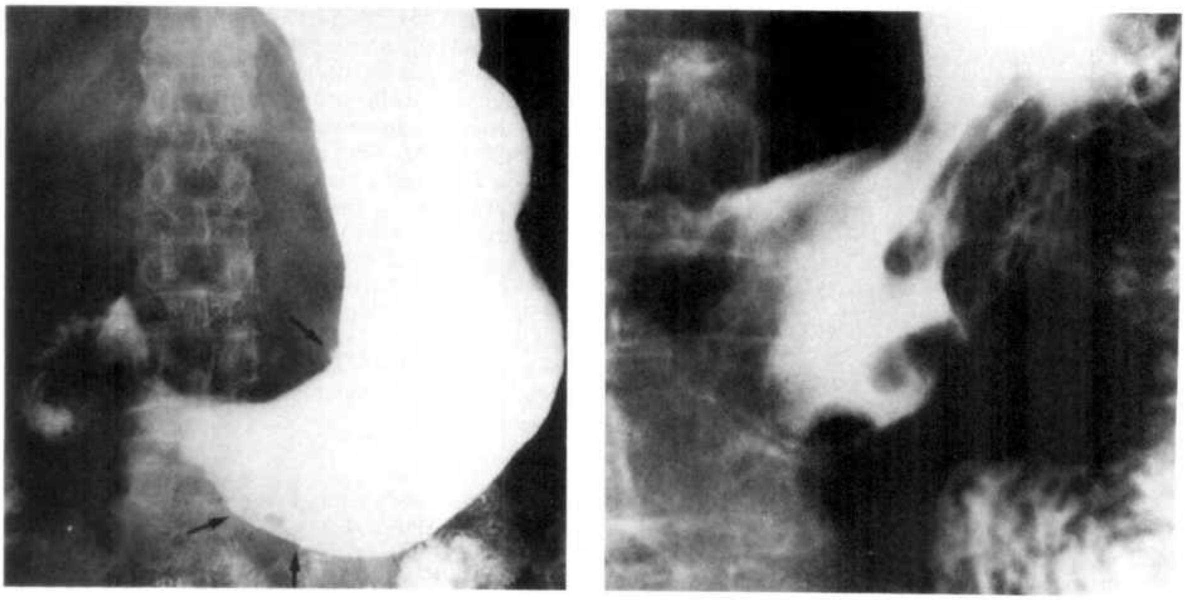

FIG. 2.

(A) Radiograph of stomach showing gastric ulcer on the lesser curvature and multiple polypoid nodules in the antrum (arrows). (B) Spot view of antrum of the same patient, showing multiple nodulations.

demarcated, showing variable degrees of osteoblastic and osteolytic changes. These may be widespread in many bones, becoming more common with progession of SMCD. The circumscribed lesions are few in number and are usually well demarcated. They occur less frequently than the diffuse lesions (1 : 3) and are seen often in patients with a favourable prognosis. These skeletal changes are not unique to SMCD and similar appearances may be found in myelofibrosis with myeloid metaplasia, leukaemias, Paget's disease, Hodgkin's disease, metastatic cancer, osteopetrosis and fluoride-related osteosclerosis.

Radiological findings in the chest include perihilar fibrosis, diffuse interstitial fibrosis throughout both lung fields, and fibrotic, nodular densities (Sagher & Even-Pat, 1967). Changes in the ribs and vertebral column may also be seen.

Significant changes in the gastrointestinal tract are

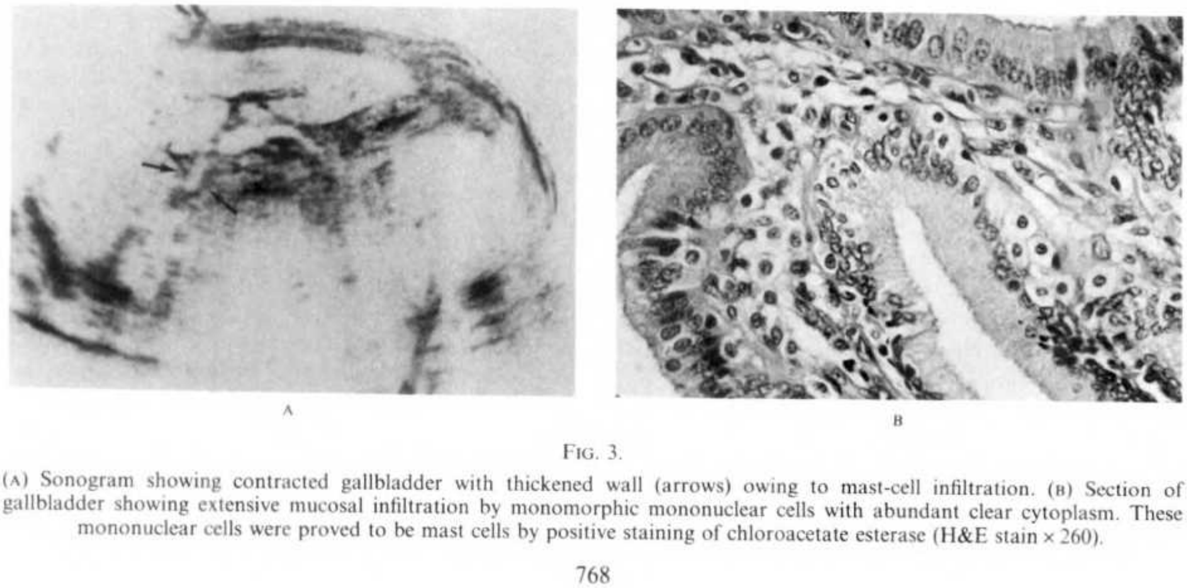

FIG. 3.

(A) Sonogram showing contracted gallbladder with thickened wall (arrows) owing to mast-cell infiltration. (B) Section of gallbladder showing extensive mucosal infiltration by monomorphic mononuclear cells with abundant clear cytoplasm. These mononuclear cells were proved to be mast cells by positive staining of chloroacetate esterase (H&E stain × 260).

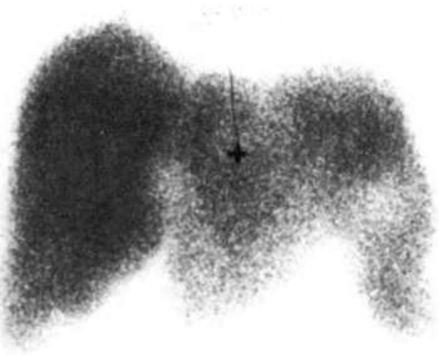

FIG. 4.
Liver–spleen scan showing hepatosplenomegaly with filling defect in the spleen.

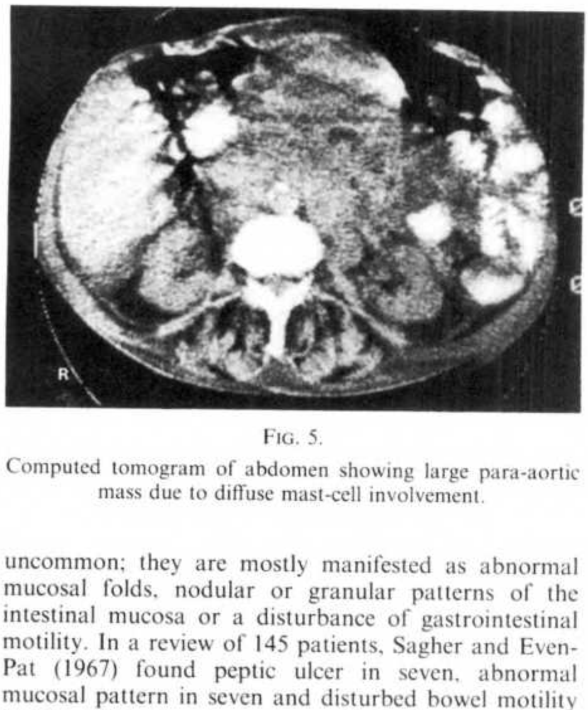

FIG. 5.
Computed tomogram of abdomen showing large para-aortic mass due to diffuse mast-cell involvement.

uncommon; they are mostly manifested as abnormal mucosal folds, nodular or granular patterns of the intestinal mucosa or a disturbance of gastrointestinal motility. In a review of 145 patients, Sagher and Even-Pat (1967) found peptic ulcer in seven, abnormal mucosal pattern in seven and disturbed bowel motility in four. These changes occur usually in the stomach and the small intestine, and occasionally in the colon and in the oesophagus. Of the several patients examined by abdominal computed tomography, lymphadenopathy was noted in three patients. The radiological appearances of the enlarged nodes in mastocytosis, however, cannot be distinguished from those in lymphoma.

In our patients with SMCD, radiological changes are similar to, but occur more frequently than, cases of mastocytosis reported in the literature (Szweda et al, 1962; Bank & Marks, 1963; Sagher & Even-Pat, 1967; Clemett et al, 1968; Dantzig, 1975; Ammann et al, 1976; Cryer & Kissane, 1976; Feldman & Isenberg, 1976; Hancock et al, 1976; Fishman et al, 1979; Lucaya et al, 1979; Tubiana et al, 1979). This is not surprising since all of our cases were known to have involvement by mast cells in many tissues and organs other than the skin. A similar reason can be given to explain the frequent involvement of visceral organs as demonstrated by radionuclide scanning and computed tomography. Despite extensive histological studies in our patients, not every lesion demonstrated radiologically could be examined histologically. However, in all the bone, liver, spleen and abdominal lymph-node samples examined histopathologically, involvement by mast cells was noted. It is a reasonable assumption that the lesions demonstrated radiologically in these tissues were the result of tissue infiltration by mast cells. In the gastrointestinal tract, we were not able to demonstrate mast cell aggregates consistently in the stomach or small intestine, although we found increased numbers of mast cells scattered throughout these tissues. Some of the lesions, such as oesophagitis and gastric or duodenal ulcers, may be related to the effects of chemical mediators released by the mast cells and not to mast-cell infiltration *per se*. In other instances, changes such as diverticulosis in the colon may be coincidentally present in SMCD.

Abnormal radiological features are often present in SMCD. These findings are characteristic of, but not unique to, SMCD. When carefully interpreted, along with the clinical presentation, they may initiate the suspicion of SMCD and indicate precisely the sites of involvement by the mast cells. Radiological findings are valuable for both the diagnosis and assessment of SMCD. In a patient who presents with signs and symptoms of systemic disease with or without those of hyperhistaminaemia (peptic ulcer disease and hyperactivity), the detection of skeletal lesions, retroperitoneal lymphadenopathy and hepatosplenomegaly by radiological studies should reinforce the need to consider haematological disorders, including SMCD.

ACKNOWLEDGMENT

We thank the physicians who supplied us with clinical, histological and follow-up information on their patients and Mr A. J. Janckila, E. J. Jorgensen, Ms S. James, Ms J. Haynes and Ms S. Brown for technical assistance. Also, thanks to the Academic and Professional Development Service for supplying the clerical support to complete this manuscript.

This study was supported in part by a research grant from the Research Service of the Veterans Administration, Washington, D.C.

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# Correction

*Wilhelm Conrad Röntgen. His life and the new kind of rays.* By Thomas J Deeley, pp. 79, 1986 (Tenovus Cancer Information Centre, Cardiff).

Will readers please note that the price of this book is £2.50 and not £1.50 as stated in the heading to the review on page 454 of the May issue of the *British Journal of Radiology.*

1987, *The British Journal of Radiology*, 60, 771–773 AUGUST 1987

# Case reports

## Gallbladder carcinoma in association with polyposis coli

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(*Received June 1986 and in revised form October 1986*)

Polyposis coli is an autosomal dominant disorder characterised by the development of multiple adenomatous polyps throughout the colon. The propensity of these polyps to undergo malignant change is well known. Gardner's syndrome (Gardner, 1951) originally comprised polyposis of the colon, skeletal osteomas and soft-tissue tumours but many other lesions have been reported, including malignant tumours of the central nervous system and thyroid gland (Bussey, 1972). Periampullary tumours—carcinomas of the pancreas, duodenum and ampulla—are found in as many as 12% of patients with polyposis coli (Harned & Williams, 1982). There have been recent reports of adenocarcinoma of the biliary system occurring in patients with polyposis coli: three cases of bile duct tumours and two cases of gallbladder carcinoma (Burney & Assor, 1976; Lees & Hermann, 1981; Jarvinen et al, 1983; Bombi et al, 1984). This association has not been described previously in the radiological literature. A case of gallbladder carcinoma in a patient with polyposis coli is reported and the ultrasound findings discussed.

### CASE REPORT

A 47-year-old woman presented with a 2-day history of right upper quadrant pain, nausea and vomiting. Fourteen years earlier she had undergone total colectomy for polyposis coli. Her sister, two children and cousins were also known to be affected with polyposis coli. Examination showed that she was not jaundiced, was afebrile and had a negative Murphy's sign. Laboratory examination showed a normal white-cell count but mildly abnormal liver function tests (SGOT 77 U/l, alkaline phosphatase 167 U/l). The clinical differential diagnosis included cholecystitis and peptic ulcer disease. A plain abdominal radiograph and upper gastrointestinal endoscopy were normal. Ultrasonography showed a complex mass of heterogeneous echoes filling the gallbladder (Fig. 1) which did not change with alteration in the patient's position. There was no acoustic shadowing to indicate the presence of gallstones and the sonographic findings were considered highly suspicious of gallbladder carcinoma. The patient continued to have upper abdominal pain and developed an elevated amylase level of 3000 U/l 3 days after the initial ultrasound examination. Repeat abdominal ultrasound showed a normal pancreas but no change in the appearance of the gallbladder (Fig. 2). Clinically the patient was thought to have chronic cholecystitis and was referred for surgery.

At operation the gallbladder appeared grossly normal and there was no evidence of metastatic disease. Cholecystectomy was performed together with resection of a single node at the gallbladder neck. Examination of the mucosal surface of the gallbladder revealed marked thickening with two distinct nodules. The remainder of the lumen was filled with sludge, and no stones were found. One nodule measured 1.2 cm and was fungating. Beneath this nodule the wall of the gallbladder was thickened and measured 0.8 cm compared with 0.3 cm in the normal areas (Fig. 3). Histology showed a moderately differentiated adenocarcinoma with abundant mucus production. The tumour extended through the entire musculature into serosal fat. The smaller nodule measured 0.7 cm and showed proliferation of complex tubular glands consistent with a polypoid adenoma. The resected lymph node showed hyperplastic changes only.

### DISCUSSION

In polyposis coli the polyps are not present at birth but appear by adolescence. Without surgery two-thirds of patients develop colon carcinoma by the age of 38

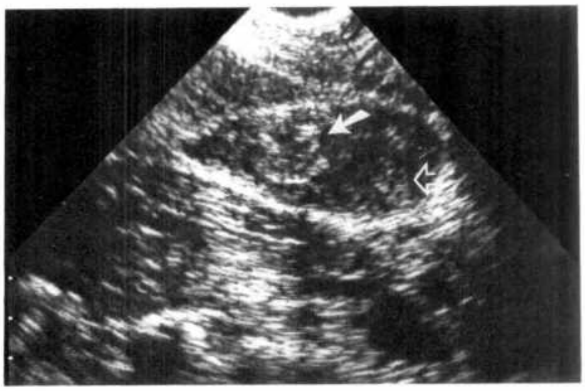

FIG. 1.

Longitudinal scan of the gallbladder shows the lumen to contain complex echoes. Note larger polypoid mass (solid arrow) which proved to be a carcinoma, and smaller polypoid mass (open arrow) which proved to be an adenoma.

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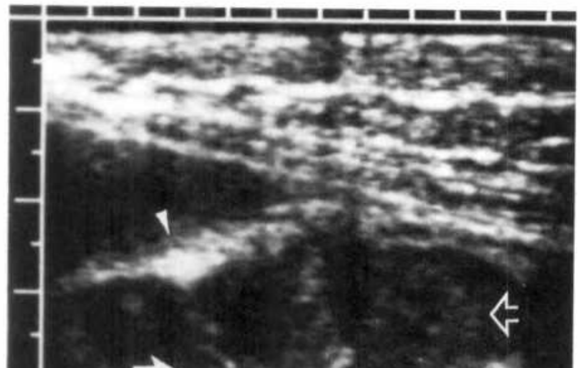

FIG. 2.

Repeat ultrasound 2 days later with high-resolution technique shows no significant interval change. Note the two polypoid masses (arrows) and focal wall thickening (arrowhead).

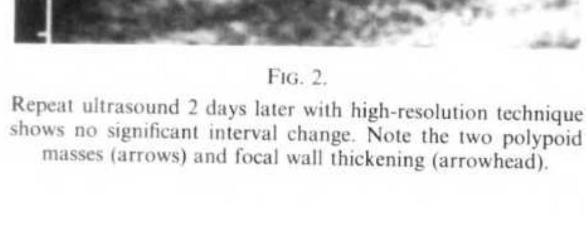

FIG. 3.

Surgical pathology specimen of sectioned gallbladder demonstrates the two masses identified at ultrasound: polypoid carcinoma (solid arrow) and adenomatous polyp (open arrow), together with focal wall thickening (arrowhead).

years and therefore total proctocolectomy or colectomy with ileo-rectal anastomosis is advocated by the age of 21 years. There is an increased incidence of periampullary tumours in those patients who have duodenal polyps. In this case the presence of an adenomatous polyp in the gallbladder in addition to the carcinoma suggests that gallbladder carcinoma may also be associated with benign polyps which may be pre-malignant.

Patients with polyposis coli appear to have a genetic predisposition to carcinoma. Now that these patients are undergoing early prophylactic colectomy it is important to follow them closely and to search for other neoplasms. Six-monthly follow-up with proctoscopy is advised to screen for malignant change in the rectum. Regular upper gastrointestinal barium studies and/or endoscopy have been advocated for early detection of periampullary tumours. Reports of gallbladder carcinomas associated with polyposis suggest that ultrasound examinations should also be routinely performed. In this case we examined the gallbladders of the patient's children who also had polyposis coli, but no abnormalities were detected.

Carcinoma of the gallbladder is very difficult to diagnose clinically in the early stages as the patient is often asymptomatic. Ultrasound is especially useful in assessing these patients as it is a rapid, accurate and non-invasive method of examining the gallbladder. When clinical signs such as jaundice and pain are present, the ultrasound findings in carcinoma of the gallbladder are commonly those of a large mass replacing or surrounding the gallbladder (Weiner et al, 1984). Liver metastases and lymphadenopathy around the porta hepatis or distal common bile duct may also be demonstrated. Gallstones are present in 73–98% and calcification of the gallbladder wall may be found in up to 25% of cases (Bevan, 1973; Do Carmo et al, 1978). Unfortunately, at this point there is no effective therapy for this condition (Piehler & Crichlow, 1978). At an earlier stage a mass protruding into the gallbladder or diffuse asymmetric thickening of the gallbladder wall may be seen. Gallbladder wall thickening is frequently seen in chronic cholecystitis but the presence of irregular or nodular thickening is suspicious of tumour. Discovery of the lesion in its nodular form (before extension from the lumen) dramatically improves patient survival.

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# Breast "abscess": an unusual complication of catheterisation of the subclavian vein

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(*Received July 1986 and in revised form October 1986*)

The insertion of catheters into the subclavian vein to gain central venous access may be complicated by catheter sepsis, pneumothorax, pleural effusion, brachial plexus injury, mediastinal haematoma and malposition of the cannula. We describe an unusual complication of this procedure: cannulation and rupture of the internal mammary vein.

## CASE REPORT

A 25-year-old woman with homozygous sickle-cell disease had a polyvinyl catheter inserted into the left subclavian vein under local anaesthesia. An antero-posterior (AP) chest radiograph was interpreted as showing patchy consolidation throughout both lung fields and the catheter located within the superior vena cava (Fig. 1). The catheter functioned satisfactorily for 7 days, but on the eighth day she complained of right-sided pleuritic chest pain; a second chest radiograph was unchanged. Two days later she complained of intense chest pain when drugs were injected through the catheter and she was tender across the medial half of the right breast. The following day she developed a fluctuant swelling in the breast which was diagnosed as an abscess and drained with release of serosanguinous fluid, sterile on culture. Two days later, clear fluid began to drain from the wound at a rate proportional to the flow of fluid into the subclavian catheter. Contrast medium

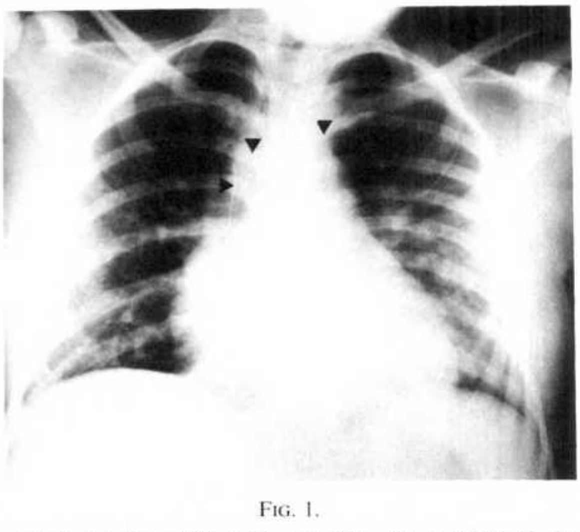

FIG. 1.

Antero-posterior radiograph showing the position of the catheter in the superior mediastinum (arrowheads).

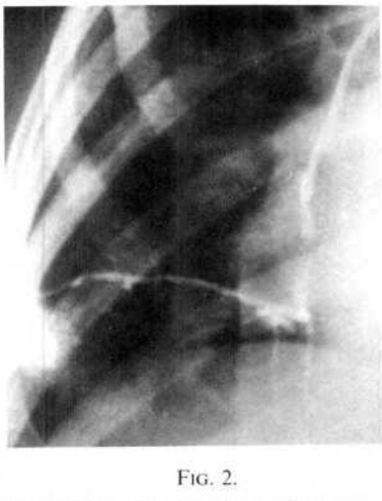

FIG. 2.

Radiograph showing the right internal mammary vein and veno-cutaneous fistula outlined by contrast medium.

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(Niopam 200) injected into the catheter showed that it was lodged in the right internal mammary vein, from where the medium tracked through the chest wall into the breast "abscess" (Fig 2). The discharge from the breast ceased after withdrawal of the catheter and the wound healed rapidly.

## DISCUSSION

Inadvertent cannulation of an internal mammary vein is a rare event and we have found only three reported cases: Gilday and Downs (1969) found only one case in a series of 200 patients undergoing subclavian vein catheterisation compared with 30 cases of catheter malposition in the jugular veins. Oakes and Wilson (1975) reported another patient who developed an anterior chest wall abscess after 10 days, heralded by radiological signs of bilateral pleural effusions and interstitial oedema. A third patient complained of right-sided chest pain made worse by the injection of drugs through the catheter (Finch, 1976).

Although malposition of a catheter in an internal mammary vein is unlikely to be detected on an AP chest radiograph, it would be impractical and expensive to do lateral views on all these patients. Finch (1976) suggests that if the catheter lies lateral to the mediastinal shadow, fluoroscopy with contrast-medium injection will readily demonstrate that it lies in an aberrant position. Asymptomatic cannulation of this vessel may occur more frequently and should be considered as a cause of chest pain or tenderness over the anterior chest wall in patients with a subclavian catheter.

## ACKNOWLEDGMENTS

We thank Mr J. W. L Fielding, F.R C.S. for allowing us to report this case and Miss P. Cole for typing the manuscript.

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1987, *The British Journal of Radiology*, 60, 775–776 AUGUST 1987

# Case of the month

## Asymptomatic abdominal mass in a child

By D. G. Richards, M.R.C.P., F.R.C.R., A. J. Stafford, F.F.R., R.C.S.I. and *J. E. DeMaria, F.R.C.P.(C.)

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(*Received September 1986*)

A 20-month-old boy was noted to have an abdominal mass while being bathed by his father. There were no symptoms related to the mass and no past medical history of note, although the grandmother had commented on several occasions since his birth that the child was unusually "pot-bellied".

On examination, a large, left-sided abdominal mass was identified. This was non-tender, ballottable and extended across the midline. There were no other positive physical findings. Chest radiograph, blood count, urea and electrolytes, urinalysis and 24 h urinary vanillyl-mandelic acid analysis were all normal.

A transverse abdominal ultrasound scan through the upper abdomen (Fig. 1) shows a large, multilobulated cystic mass with highly echogenic septa. No normal renal tissue could be seen on the left. The right kidney was normal.

A computed tomogram (Fig. 2A) confirms that the mass is in the kidney, and is displaying well defined, normally functioning remaining renal tissue in front of and to the right of the midline (Fig. 2B). The renal capsule is intact.

What is your diagnosis?

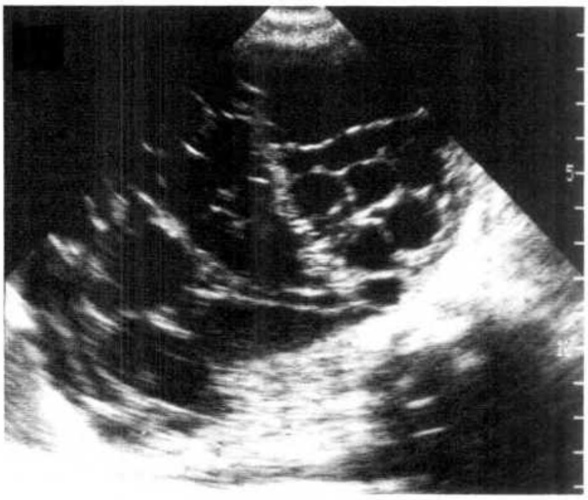

FIG. 1.

Transverse ultrasound scan through the left upper abdomen.

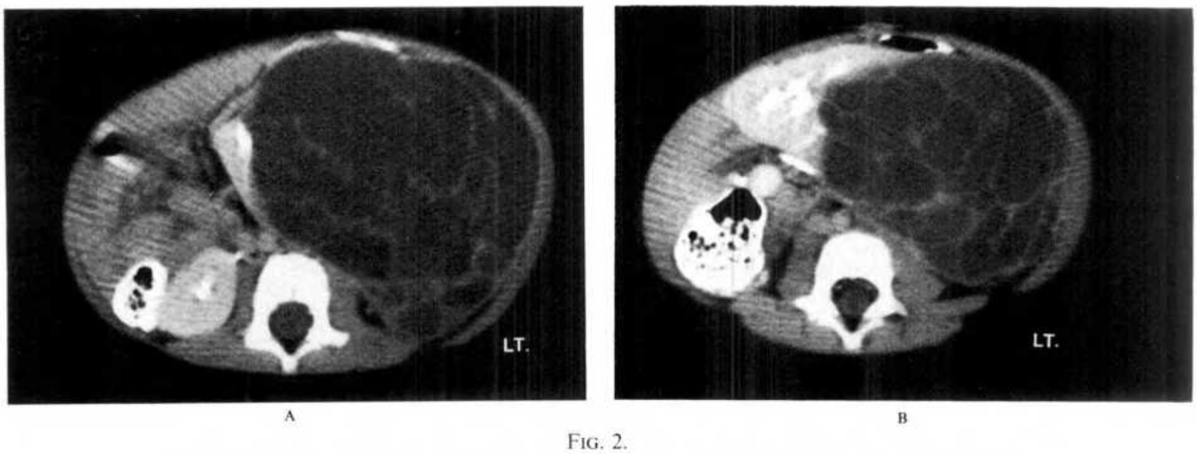

FIG. 2.

Enhanced computed tomograms through the upper abdomen, (A) at a higher level than (B).

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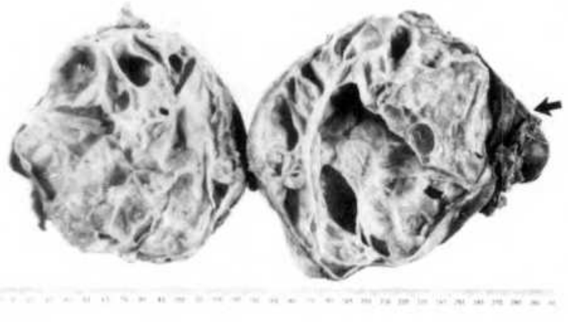

FIG. 3.

Nephrectomy specimen. Arrow indicates the remaining normal renal tissue.

A unilateral multicystic kidney in a child may be due to renal dysplasia, which is seen more often on the left side and is associated with malformations in the opposite kidney and other organs, or with the unilateral multilobular cyst, which has no associated abnormalities (Witten et al, 1977).

In our patient, a large renal mass was encountered at surgery, but despite its size it was relatively easily removed, with minimal blood loss. The nephrectomy specimen measured 13 cm × 7 cm × 14 cm and shows multilocular cysts of varying size with only a small amount of normal renal tissue remaining (Fig. 3). Histological examination showed that the cysts were lined by attenuated epithelium with a "hob-nail" appearance. The intervening stroma showed no evidence of sarcomatous or nephroblastomatous elements.

The clinical presentation, radiological appearances and pathological features are typical of a multilocular cystic nephroma, also known as multilocular cyst of the kidney. This uncommon, non-familial renal neoplasm is usually benign and unilateral but occasionally metastasises and is rarely bilateral (Madewell et al, 1983). It is not associated with cystic change in other organs. Treatment is usually by nephrectomy, as local excision can sometimes be associated with recurrence. The disease affects, predominantly, males under 2 years and females in the fifth and sixth decades. Presentation in childhood is usually with an asymptomatic abdominal mass.

The plain radiograph in this condition can occasionally show curvilinear calcification in addition to the mass, and intravenous pyelography usually shows a renal mass-lesion indistinguishable from a Wilms' tumour. Herniation of the tumour mass into the renal pelvis may occur, causing hydronephrosis and haematuria. In the few cases where cyst puncture has been performed, injection of contrast medium has shown that the individual cysts do not communicate.

Multilocular cystic nephroma needs to be differentiated from other "cystic" renal masses of childhood, which include the commoner hydronephrosis and multicystic dysplastic kidney, and the rarer adult polycystic disease as well as simple renal cysts (Grossman et al, 1983). Ultrasonography should be the initial imaging method (Kirks et al, 1985) and will normally differentiate these lesions, bearing in mind that a sonogram will show communication between dilated calyces, infundibula and pelvis in hydronephrosis and absence of normal renal tissue in multicystic dysplasia. In adult polycystic disease, the condition is bilateral and there is usually a family history. Simple cysts have the same appearances as in adults. Wilms' tumour can contain cystic spaces due to haemorrhage and tumour necrosis (Beckwith & Kiviat, 1981) but the overall appearance is of a solid lesion.

Computed tomography has a secondary role in imaging of renal masses in childhood (Kuhn & Berger, 1981) but can often clarify the diagnosis, as in the present case.

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1987, *The British Journal of Radiology*, 60, 777–779 AUGUST 1987

# Short communication

## Short and long fractionated schedules in radiotherapy and a proposed improvement

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(*Received January 1987 and in revised form March 1987*)

This paper compares the "northern UK" practice in radiotherapy (of using short overall times and a small number of relatively large fractions) with the "southern UK and elsewhere" practice (of using overall times as long as 6–7 weeks and 30–35 fractions of 2 Gy).

Neither of these methods is optimal. The "northern" schedule uses doses per fraction which are, in principle, too large, but this calculable disadvantage is offset by a usefully short overall time, at least in tumours which proliferate fast. The "southern" schedule uses overall times which may be too long for the fast-proliferating tumours, but this disadvantage is offset by the use of smaller doses per fraction, which spare late reactions more than they spare early reactions or tumour cell kill.

Because both types of existing schedule are predictably suboptimal, although for different reasons, it can be predicted that neither type of schedule will show a distinct advantage over the other in clinical results. We are now beginning to understand the biological reasons and to be able to suggest steps forward (Thames et al, 1983). Both types of schedule could obviously be improved by the conceptually simple step of giving 30 or 32 fractions at the rate of two fractions (2 F)/day in an overall time of 3 weeks This schedule would not increase the workload on treatment machines or staff above existing levels in the south of the UK.

It is important that the intervals between the two fractions should not be less than 6 h, in order to allow full repair of sublethal damage in normal tissues, especially in the late-reacting tissues (Thames, 1984; Fowler, 1986a) This is why 2 F/day will be more convenient within a normal working day than 3 F/day.

It is important to adjust the total doses In the southern schedules the total doses should be reduced from those used in 6–7 weeks, to allow for the proliferation which occurs in early-responding normal tissues between 3 weeks and 6–7 weeks. It is also important that the total dose in northern schedules be increased to allow for the reduced effectiveness of the smaller-sized fractions (in the same overall time of 3 weeks)

### *Calculation of doses in 32 fractions in 21 days starting from 16 fractions in 21 days*

The latter correction is the easier of the two to make: the effect of fraction size can be reliably calculated using the linear quadratic formula if there is no change in overall time For example, the change from 16 daily fractions in 21 days to 32 fractions given twice a day in the same 21 days requires the increase of total dose from 49, 50, 52 5 or 55 Gy (as 16 F/32 days) to 54 7, 55.9, 58.9 or 61.9 Gy respectively for equal early damage, *i.e.* fraction sizes of 1.71–1 94 Gy, as listed in Table I The actual total doses used will of course depend on the volume irradiated This calculation assumes only that $\alpha/\beta = 10$ Gy, as an average value for the early reactions (Thames et al, 1982; Withers et al, 1982). The calculation is based on the linear quadratic relation:

$$\text{effect} = n(\alpha d + \beta d^2)$$

where $d$ is the dose per fraction and $n$ is the number of fractions Thus, for two schedules causing equal biological effects and of the same overall time (Fowler, 1984):

$$n_1(\alpha d_1 + \beta d_1^2) = n_2(\alpha d_2 + \beta d_2^2)$$

It is expected that early reactions in normal tissues and local tumour control would then both be the same as with the 16 F/21 days schedules

The late effects, however, should depend only upon total dose and dose per fraction, not upon overall time (Arcangeli et al, 1974), so they should all be less severe for the total doses calculated above The *late-responding tissues* in the examples above would be underdosed by 9.85%, 9.86%, 9.92% and 10 0% respectively, compared with the corresponding schedules given as 16 F/21 days. For this calculation $\alpha/\beta = 3$ Gy was assumed, again as an average value, to represent late effects (Thames et al, 1982, 1983). This sparing of late injury is one of the advantages of hyperfractionation, in addition to the advantages of the short overall time of 3 weeks. Alternatively, in schedules where *the acute effects are not too severe*, the total dose might be increased somewhat (by up to 10%) without the expectation of worse late damage than the present 16 F/21 days schedules.

### *Calculation of doses in 32 fractions in 21 days starting from 30–35 fractions in 6–7 weeks*

Compared with 32 F/43 days, the shortening to 32 F/21 days would save 22 days of overall treatment time, thus allowing less time for tumour-cell proliferation If the doubling time of the clonogenic cells is shorter than about 6 days (Steel, 1977; Fowler, 1986b) then fewer cells (a factor of 10) would have to be killed. If there are nine or 10 logs (factors of 10) of cells to be killed in a tumour, one log less would mean an effective increase in tumour dose of about 10% in tumours which proliferate as fast as this (Trott & Kummermehr, 1985; Fowler, 1986b) No difference in average incidence of early normal-tissue damage would be expected provided that the total doses were reduced from the usual 60–66 Gy to the range given above (54.7–61.9 Gy).

The calculation of total doses for a 32 F/21 days schedule which would give the same early normal-tissue reactions as 30–33 fractions in 6–7 weeks requires a subtraction to allow for the effect of proliferation. Skin proliferation does not begin in human patients until 3.5–4 weeks (Turesson & Notter, 1984) and mucosal proliferation until 2.5–3 weeks after starting fractionated radiotherapy, but may then become as fast as the

TABLE I

EARLY REACTIONS. TOTAL DOSES (AND DOSES PER FRACTION) (GY) CALCULATED TO GIVE THE SAME EARLY NORMAL-TISSUE REACTIONS IN A 2 F/DAY SCHEDULE AS IN CURRENT SCHEDULES*

| | |
|---|---|
| Starting with 16 F/21 days: | |
| 16 F/21 days | 32 F/21 days† |
| 49.0 (16 × 3.063) | 54.67 (32 × 1.708) |
| 50.0 (16 × 3.125) | 55.87 (32 × 1.746) |
| 52.5 (16 × 3.281) | 58.88 (32 × 1.840) |
| 55.0 (16 × 3.438) | 61.92 (32 × 1.935) |
| Starting with 30–33 F/6–7 weeks | |
| 30–33 F/6–7 weeks | 32 F/21 days† (after subtracting 5 × 2 Gy fractions for proliferation) |
| 60.0 (30 × 2.0) | 51.66 (32 × 1.614) |
| 62.0 (31 × 2.0) | 53.47 (32 × 1.671) |
| 64.0 (32 × 2.0) | 55.26 (32 × 1.727) |
| 66.0 (33 × 2.0) | 57.04 (32 × 1.782) |
| | (After subtracting 3 × 2 Gy fractions for proliferation) |
| 60.0 (30 × 2.0) | 55.26 (32 × 1.727) |
| 62.0 (31 × 2.0) | 57.04 (32 × 1.728) |
| 64.0 (32 × 2.0) | 58.80 (32 × 1.837) |
| 66.0 (33 × 2.0) | 60.55 (32 × 1.892) |

*Assuming a representative value of $\alpha/\beta = 10$ Gy

†If 30 F/18 days were used, the total doses would be about 1% lower.

TABLE II

LATE REACTIONS: EQUIVALENT TOTAL DOSES (GY) CALCULATED FOR LATE REACTIONS IN NORMAL TISSUES*

| Present schedule | Total doses in 32 fractions, assuming an $\alpha/\beta$ value of. | | | |
|---|---|---|---|---|
| | 2 Gy | 3 Gy | 4 Gy | 5 Gy |
| Starting from 16 F/21 days | | | | |
| 49.0/16 F | 62.67 | 60.67 | 59.17 | 57.99 |
| 50.0/16 F | 64.04 | 62.02 | 60.48 | 59.28 |
| 52.5/16 F | 67.48 | 65.3 | 63.78 | 62.52 |
| 55.0/16 F | 70.93 | 68.77 | 67.10 | 65.77 |
| Starting from 30–33 F/6–7 weeks | | | | |
| 60.0/30 F | 61.30 | 61.11 | 60.96 | 60.86 |
| 62.0/31 F | 62.66 | 62.56 | 62.49 | 62.44 |
| 64.0/32 F | 64.0 | 64.0 | 64.0 | 64.0 |
| 66.0/33 F | 65.32 | 65.42 | 65.49 | 65.55 |

In schedules where these doses are higher than those in Table I, the early reactions will be the dose-limiting ones.

**i.e.* Ignoring overall time, and assuming representative values of $\alpha/\beta$ ranging from 2 Gy to 5 Gy

equivalent of adding 6–10 Gy per week after the third week of radiotherapy (Denekamp, 1973). Nevertheless, a reduction in total dose by only about 10 Gy was found to be appropriate in the accelerated fractionation schedules of Svoboda (1978), who used doses per fraction which included conventional sizes in overall times of only 10–12 days. Therefore the most appropriate procedure seems to be to subtract five of the 2 Gy fractions from the 30–33 original fractions and to recalculate from the resulting 25–28 fractions to the required 32 fractions, which is a small correction. The result is shown in the bottom part of Table I. It is obvious that lower doses are estimated by this procedure than by starting from the known doses in 16 F/21 days and correcting only for fraction size. This discrepancy means either that there is less proliferation occurring in human normal tissues during fractionated radiotherapy than is expected from animal experiments (Denekamp, 1973; Moulder & Fischer, 1976), or that the present 16-fraction schedules are biologically more damaging than the present 6-week schedules, unless the latter approach 70 Gy in 35 fractions. An alternative calculation, subtracting only three of the 2 Gy fractions before correcting from the 27–30 fractions to 32 fractions, is also shown in Table I. It is impossible to decide between these on grounds of logic, but a dose-searching trial would quickly show which total doses were appropriate, because early reactions will be dose-limiting.

*Late injury* is not expected to depend upon overall time, because there is little or no proliferation in these tissues during the period of 3–7 weeks. Therefore it can be easily compared in the two schedules. 55 Gy in 16 fractions is then about equally as effective as 70 Gy in 35 fractions (+7% to −5% over the range of $\alpha/\beta$ values 2–5 Gy). If the total dose in 16 fractions is reduced to 50 Gy, this should give similar late injury to about 60 Gy in 30 fractions (+7% to −3% over the same range of $\alpha/\beta$ values). The corresponding total doses required for 32 fractions would be about 69 Gy and 64 Gy respectively for the same late injury as in the existing 16-fraction schedules, the doses computed for equivalent *early* reactions are lower than 69 Gy and 64 Gy (Table I) so that late reactions should not be limiting.

Table II shows that if late reactions are assumed to be held the same as in existing schedules, larger total doses would be required than those proposed in Table I. If the doses shown in Table I are used, the early reactions should be the dose-limiting ones, and dose levels could safely be selected by observing the early reactions.

*Summary of gains to be expected from 32 fractions in 16 days*

First let us consider the gains to be expected starting from the northern UK practice of 16 F/21 days. If the number of fractions is doubled to two fractions per day in the same overall time, and the total doses listed above are used (54.7–61.9 Gy) so that doses per fraction fall to about 1.7–1.9 Gy, then a *predictable sparing of late reactions should occur*, as if the effective dose to late-responding normal tissues had been reduced by about 10%. The early reactions and local tumour control should be unchanged, in fact the early reactions would be the dose-limiting factor. *If the early reactions permitted an increase of total dose* (of up to 10%), that increase would then be a real increase in effective dose to the tumours, and the late reactions would rise again to become as they are with current 16 F/21 days schedules. In the most favourable circumstances, local control might then rise 10–15% (Fowler, 1986b). However, early reactions in treatments to full tolerance would not permit this increase above the doses in Table I.

Secondly, let us consider the gains to be expected relative to a 6–7-week schedule consisting of 32 fractions in 43 days. Shortening the overall time by 22 days obviously allows less proliferation of tumour cells. *If the doubling time of clonogenic cells in the tumour is shorter than about 6 days* (Steel, 1977; Trott & Kummermehr, 1985; Fowler, 1986b) there would be a factor of 10 fewer cells to kill, *i.e.* one log in nine or 10 logs of tumour cells. This is equivalent to an effective increase of tumour dose by about 10%, similar to the gain described above. It should be achieved with no change in the early reactions in normal tissues and with a small decrease in late reactions, if total doses similar to those in Table I are used The early normal-tissue reactions would become dose limiting and would soon be observed. Again, *if the early normal-tissue reactions were found to permit an increase of total dose* (of up to 10%), that increase would be a second and real increase in tumour dose, regardless of cell doubling times, and the late reactions would rise again to the current values The result of this second stage would be to put up the effective doses in fast-proliferating tumours by as much as 20%, and in slowly proliferating tumours by up to 10% As above, early reactions might not permit this increase above the doses in Table I.

One of the interesting conclusions from these calculations is that the current 16 F/21 days schedules are probably causing more biological effect than current 6-week schedules by about 10% (in terms of dose); this comment is not expected to pass without debate Therefore there appears to be more to gain from shortening the 6–7-week schedules using 2F/day with total dose at a new optimum level. Even without the second-stage gain, both types of schedule appear to be capable of improvement by about 10% in terms of therapeutic ratio.

Starting from either schedule and changing to 32 F/21 days requires a dose-searching programme (Phase I trial) to establish just where, in the range of doses listed, the early reactions become really dose limiting for particular sites and volumes. It is one of the advantages of the smaller doses per fraction (1.7–1.9 Gy) that late reactions are not expected to be the dose-limiting ones when shorter overall times are used.

In conclusion, the importance of maintaining minimum intervals of at least 6 h must be re-emphasised (Thames, 1984; Thames et al, 1984; Fowler, 1986a)

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# Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

## Financial considerations of contrast media in intravenous urography

The Editor—Sir,

It is recommended that patients requiring intravenous urography (IVU) who are at increased risk of adverse reaction to contrast media should always be injected with a low-osmolar contrast medium (Grainger, 1984) The main disadvantage of this wise policy is financial because of the high cost of the low-osmolar media.

In a recent study carried out at Lodge Moor Hospital, Sheffield, 67 consecutive patients with neurogenic bladder dysfunction associated with spinal paralysis (65 male and two female, mean age 35.7 years and range 17–65 years) had IVU for routine examination of the upper urinary tract. Fifty millilitres of Urografin 325 (Schering AG) was injected intravenously in all patients. A full-length radiograph of the abdomen was taken before and 15 minutes after the injection No compression was used Delayed radiography and tomography of the kidneys were carried out if necessary The examinations were reviewed by both authors independently and found to be of good diagnostic quality in 65 patients (96.9%). Tomography of the kidneys was necessary in only three patients (4.5%). The urogram was unsatisfactory and not diagnostic in the remaining two patients (3.1%). Forty-nine examinations (73 1%) were normal. The remainder demonstrated abnormalities which included renal scarring, stones, and dilatation of the pelvicalyceal system and ureters Twenty patients (29 8%) developed minor reactions to the contrast medium, the commonest reaction being a feeling of warmth in six patients (9.3%). No major reactions occurred in this study

We found Urografin 325 to be a cheap, safe and satisfactory contrast medium for IVU. The hospital price of a 50 ml vial is £2 23 The only other medium of comparable price and efficacy in IVU is Sodium "Uromiro" 300 (Bracco; £2.04 for a 50 ml vial) We have no experience with this medium but Davies et al (1985) reported that it is nearly as good as Conray 420 (May & Baker Ltd; £3.44 for a 50 ml vial) for urography. We are not aware of any other contrast media which are satisfactory for IVU and cheaper than Urografin 325 or Sodium Uromiro 300.

We would like to suggest that the use of a cheap but relatively safe and satisfactory contrast medium such as Urografin 325 or Sodium Uromiro 300 routinely for IVU will have financial benefits, saving at least £1 per examination if they are used instead of some of the commonly used media If such apparently insignificant savings are multiplied by the large number of intravenous urograms carried out annually in the UK (about one million examinations in 1983) several hundred thousand pounds could be saved This saving would help towards the cost of the expensive low-osmolar media which must be used in patients at high risk. With current financial constraints every possible saving should be attempted

Yours, etc ,
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(*Received February 1987*)

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## An evaluation of radionuclide tomography in detecting renal space-occupying lesions

The Editor—Sir,

We read with interest the paper by Williams et al (1986) as we are also currently evaluating the clinical usefulness of radionuclide tomographic imaging of the kidneys and its advantages over the conventional planar gamma-camera imaging in detecting space-occupying lesions We chose $^{99}\mathrm{Tc}^{m}$-gluconate (600 MBq) for our studies as it allows us to perform three studies following a single injection The initial first-pass perfusion study is useful in differentiating vascular from non-vascular lesions The static images acquired are of sufficiently good quality when compared with those of DMSA scans Tomographic studies are usually performed 30–60 min after the initial injection In addition, we attempt to assess the vascularity of the lesions by repeating the tomographic studies using a blood-pool imaging technique.

We have so far examined 28 cases in which renal space-occupying lesions were suspected following intravenous urography Subsequent ultrasonography, radionuclide scans (including tomographic studies) and operative findings have confirmed the diagnosis of carcinoma in eight cases, cysts in 11 and no lesion in nine. As the number of cases studied is still relatively small, we have not yet performed a statistical analysis to confirm or disprove any significant advantage of the tomographic method over the conventional imaging. However, it is our impression that all the lesions detected by the tomographic method were visualised by conventional planar imaging, although in two cases the lesions were undoubtedly better demonstrated by the tomographic method.

In order to assess the vascularity of the lesion further, we have on 16 occasions repeated the tomographic studies with the "blood-pool" technique. We administered 800 MBq of $^{99}\mathrm{Tc}^{m}$-pertechnetate 20 min after cold stannous pyrophosphate in order to effect *in-vivo* labelling of red blood cells. Encouraging results have emerged In one case we were impressed by the clarity of the tumour circulation demonstrated by this technique, which corresponded very well with the finding at operation Obviously it is too early to make any firm comment about this technique and further research is continuing to evaluate its potential

Our overall impression of radionuclide tomographic imaging of the kidney concurs with the comments made by Dr Williams It does not appear to improve the detection rate of space-occupying lesions. However, in certain cases it helps to demonstrate the lesion more clearly The full potential of radionuclide tomography of the kidney in clinical practice needs to be further explored.

Yours, etc.,
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(*Received October 1986*)

### *Authors' reply*

THE EDITOR—SIR,

We welcome the interest of Dr Wujanto and colleagues from Manchester Royal Infirmary in our paper, and in the continuing search for efficient methods of diagnosing space-occupying lesions of the kidney. In our paper we concluded that emission tomography rarely contributed to the diagnosis in renal investigations. We stated, therefore, that we would in future use radionuclide imaging and ultrasonography routinely, but employ emission tomography selectively We have now reviewed the effects of introducing this protocol in 78 sets of scans, done since the previously published series, and in which we have adequate information to make an evaluation. Seventeen patients had a renal tumour, 22 had renal cysts, two had abscesses and 37 had no lesion (but this includes six with renal pseudotumours). Tomography was done on 29 occasions but the proportion having tomography decreased over the period of study from two thirds of investigations initially, before rigorous application of the protocol, to about one in five to 10 patients now.

As previously, we have found planar imaging accurate in detecting lesions of the kidney and, like O'Reilly et al (1981), have found perfusion scans helpful but not invariably so Thus, of the 17 patients with solid renal tumours, 12 showed increased perfusion, three had decreased perfusion and two were equivocal, while in 18 patients with renal cysts who had a perfusion study, 12 showed decreased perfusion and six no abnormality. Thus, in patients where no definite increase or decrease in perfusion was shown, the nature of the lesion could not be inferred The technique described by Dr Wujanto may therefore have something to contribute in the area of characterising lesions However, our approach is to perform ultrasonography with knowledge of the results of other investigations (urography and radionuclide imaging) In the series of patients mentioned above, this has been accurate in every case in differentiating between solid tumours and cysts. We have no figures for the accuracy of ultrasonography used blind, since this is rarely done in patients with possible renal masses, but suspect it would be lower. Our approach has the advantage that it can be done on the same visit as the initial investigation, rather than on a second visit which would be necessary for the blood-pool technique, and it is much less expensive than performing another tomographic scan. One area in which we have, however, found tomography to be consistently useful is in the positive identification of pseudotumours, which can mimic a space-occupying lesion on urography. These are less easily identified than cysts are by ultrasound, but can be clearly shown by emission tomography as areas of ectopic uptake of DMSA within the kidney (Williams & Parker, 1982).

Yours, etc ,
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(*Received November 1986*)

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## Developer temperature in diagnostic departments

THE EDITOR—SIR,

We report here the result of a survey made of 192 of the larger diagnostic departments spread throughout the United Kingdom, looking at the temperature at which their film processors were being run. It was found that on average they were set 2.3°C below the manufacturers' recommended level.

In order to make good this lower developing temperature, the exposure of the film has to be increased, and hence the radiation exposure of patients is also increased in a similar proportion. For the old types of film (which currently account for two-thirds of use in the United Kingdom) the increase necessitated by a reduction in processor temperature of 2.3°C is about 25%: for the newer-technology films the increase is less, at around 5–10% (Jenkins, 1980) There is thus the possibility, by merely running all developing machines at the temperatures recommended by the manufacturers, of reducing the collective radiation dose from radiography by at least 10%.

The total annual Great Britain diagnostic radiography collective dose of ionising radiation (excluding computed tomography) is estimated at 15 500 man. Sv (Shrimpton & Wall, 1986). After allowing for the dose from fluoroscopy, the reduction available by increasing the processor temperature is at least 1400 man. Sv, and this saving is obtainable at no cost.

To put this figure into context the annual calculated collective effective dose equivalent over the next 10 000 years to the United Kingdom population from the 1985 discharges to the Irish Sea from Sellafield is about 10 man. Sv. The total United Kingdom occupational exposure is estimated at 510 man Sv annually (medical workers accounting for about 1% of this) (Hughes & Roberts, 1984)

Why are film processors run at a temperature lower than that recommended by the manufacturers? In the days of hand-developing, thermostats were not as sensitive as they are today

Fluctuations of temperature were common, and base fog could increase if the temperature rose too high. This was often avoided by keeping the developer temperature a little low and increasing the developing time as necessary. When the first automatic processors appeared this "tradition" remained as thermostatic control was still relatively insensitive The desire to keep the temperature a little low still seems to persist but the reason for it is no longer present as the thermostats are now very sensitive.

Another possible reason for lowered temperature of development is to increase the contrast of the image· the contrast gradient ($\gamma$) falls with the increase in temperature. This change might be noticeable, although the variation is less marked with the new-technology films

The temperature levels recommended by the manufacturers are associated with the optimum performance of their films and processors and should be observed by the users A substantial reduction in the radiation dose to the patient is an added advantage.

Yours etc ,
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## Paget's disease of bone in Africans

THE EDITOR—SIR,

M. H. Dahniya's article on Paget's disease of bone in Africans (Dahniya, 1987) reminded me that I can recall seeing only one case of Paget's disease of bone amongst the indigenous population of the Arabian Peninsula, and this was in an Arab lady with an admixture of East African blood My observations were over a period of 20-odd years from the mid-fifties. With the number of trained observers now in the same area, it would be interesting to read further comments on the incidence of the disease, in both Eastern Arabia and East Africa.

Yours, etc.,
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# Proceedings of The British Institute of Radiology

## Radiology '87: forty-fifth Annual Congress and Scientific Exhibition, held in Southampton, April 1–3, 1987

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## Presidential Address

### THE INSTITUTE AT 90—A TIME FOR REAPPRAISAL?

R. J. Berry

*Department of Oncology, Middlesex Hospital Medical School, London*

Illustrations from the wealth of archival material in the Institute's library are used to try to recreate the excitement engendered by Röntgen's discovery and the amazing cross-fertilisation of scientific ideas to which it led. The new science of radiology was of necessity multidisciplinary from the start, and the Röntgen Society which evolved as its forum crossed social as well as scientific divides

Ninety years later, "Radiology" may be described as a fabric of interlinked disciplines. The exponents of the different fields at the outer edges of radiology appear to have little in common—and yet because they are part of the whole they have a real contribution to make to each other if only they can communicate effectively The danger to science is that as society demands more and more formal evidence of scientific and medical competence, fragmentation results as each new specialty defines its professional boundaries and speaks only to its own converts.

What role today, then, for a multidisciplinary British Institute of Radiology where membership is based on real commonality of interest, and not on professional status or advancement? The future of the Institute and, I believe, of British radiology as a contributor to the world scene, depends on our ability to achieve synthesis of that which is best and most original in all our contributing disciplines. Ninety years on, the pattern and materials of radiological endeavour have changed almost beyond recognition, but a strong Institute remains because the basic framework is right. Our strength is in our diversity; our future is in our enthusiasm.

## Growth Areas in Radiotherapy

**Chairman: Dr R. Buchanan**

The future of hyperthermia as an adjunct to radiation therapy, by G M Hahn
Can chemotherapy improve local control? By J M. A Whitehouse. No abstract received
Positron emission tomography as a marker for tumour response, by R. P Beaney
Magnetic resonance scanning as a marker for tumour response, by R. Johnson No abstract received

### THE FUTURE OF HYPERTHERMIA AS AN ADJUNCT TO RADIATION THERAPY

George M. Hahn

*Department of Therapeutic Radiology, Stanford University School of Medicine, Stanford, California, USA*

Hyperthermia is becoming widely used as an adjunct to radiation therapy The reasons for this lie primarily in the complementary nature of cell killing by X rays and by heat, although heat-induced sensitisation to X rays also plays a part Many clinical studies have demonstrated that the combination of the two modalities is more effective against tumours than either alone, data on normal tissues are more difficult to evaluate, but the general feeling of therapists is that hyperthermia causes remarkably few adverse effects. Thus, there appears to be a true therapeutic gain

A recent study has shown that two hyperthermia treatments during a fractionated course of X-ray therapy may be as efficacious in improving antitumour effects as a larger number of such treatments; hence, the economic burden of hyperthermia on the patient (or insurer) becomes quite acceptable. Successful treatment, however, depends upon ability to heat the lesion Tumour response rate is closely correlated with minimum tumour temperature Therefore, the future of hyperthermia will be determined to a large extent by the ability of physicists and engineers to develop better equipment for the heating of tumours (and for mapping of tumour temperatures) and on the ability of physiologists and physicians to use such equipment in an optimum fashion.

### POSITRON EMISSION TOMOGRAPHY AS A MARKER FOR TUMOUR RESPONSE

R P. Beaney

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Positron emission tomography (PET) is a technique that allows us to study regional tissue function in a virtually non-invasive fashion Positron emission tomography complements the essentially morphological data obtained from conventional X-ray computed tomography and magnetic resonance imaging by providing additional information on tissue perfusion and a variety of physiological, biochemical, metabolic and pharmacokinetic processes. The technique has been used to study not only the basic pathophysiology of tumours and their effects on surrounding tissue but also the physiological and metabolic effects of treatment Unlike other radionuclide scanning techniques, PET permits the measurement of the regional tissue concentration of the tracer in absolute units. Tracer kinetic models that accurately describe the fate of the administered tracers are a necessary prerequisite to the calculation of regional tissue function. Regional tissue blood flow, oxygen utilisation, glucose utilisation, amino acid uptake, blood volume, pH and capillary permeability have all been measured in various tissues, although most work has been done on the brain Preliminary work has been on the physiological effects of steroids, irradiation, hyperthermia and drugs on both neoplastic and normal tissue

## Use of Computers in the Management of Radiology Departments

**Chairman: Dr G. R. Sutherland**

The political and organisational context of information technology in the NHS, by D J Hewett
Recent developments in computer hardware, by R K. Burdge
Prospective and retrospective data searches, by H. B. Meire
Management benefits of the radiology computer, by R. M Atkinson
Pitfalls and problems with a computer X-ray system, by R. A. Owen

### THE POLITICAL AND ORGANISATIONAL CONTEXT OF INFORMATION TECHNOLOGY IN THE NHS

D. J. Hewett

*Winchester Health Authority, Hampshire*

The National Health Service (NHS) is a large and complex organisation which until 10 years ago operated in a largely unplanned and unco-ordinated way. Original construction in three distinct parts, each with separate political and organisational control processes, inhibited early development. Since the late 1960s, however, the NHS has had repeated phases of organisational upheaval, as well as great changes in the services it provides to patients Most recently, the application of management techniques borrowed from private enterprise, particularly general management, have accelerated the pace of change, so that restructuring has become continuous Continuing adaptation is found within all large organisations, so that structural permanence is no longer even desirable.

In a recent book surveying business enterprises (*The Pursuit of Excellence*), one key success factor which emerged suggests that the best organisations adapt rapidly to external changes. Adaptability is not always inversely proportional to size, but is associated with possession of a clear view of purpose. General management theory rests upon the notion that the purpose behind any complex organisation can be summed up in a single succinct statement of business objectives That central purpose may be lent detail by a hierarchy of subprocesses derived logically from it

A successful organisation will have divisions serving those subprocesses, as will the information systems which permit management to control, monitor and develop them. Information is therefore central to achievement of management objectives To take a familiar analogy, it is the physiology of the organisation. Hence information in a service-giving organisation has two roles: it records the delivery of service, and provides the data to be turned into intelligence which is used to run the organisation. Information, therefore, is a ubiquitous corporate resource, similar to finance, needing to be managed and controlled in the same way. When information is restricted to manually operated, paper systems, it will be trapped at the bottom of the organisation because it is needed to provide continuing service and cannot be expeditiously processed for use by management. Computer systems change that by profoundly altering the balance of power between service-giving and management layers This forces both to re-evaluate their relationships, communications and style. The introduction of computer systems therefore generates change which, if incorporated within an organisational development strategy, is of a rapid and radical kind.

Thinking along these lines underpins the DHSS *Framework for IT in the NHS* and has been expanded in the guidelines which support it. The Health Service Board has also sought to explore the nature of the changes which can be brought about through the six demonstration sites for resource management. One tradition of the NHS which falls casualty to this philosophy is the notion of pure clinical freedom. If the purpose of the NHS is to treat patients, then those who treat them should take the major operational decisions in the service. Doctors have not only to take managerial responsibility, but also operate within budgets and control and co-ordinate other staff. This can only be done when the resource consequences of clinical decisions are reported back to those who take them Creating such an environment is itself dependent upon a comprehensive set of information systems, centered upon patients and covering every aspect of hospital and community health services activity. Consequently, the network of systems will primarily facilitate the delivery of service, providing management information as a by-product Operational systems must therefore be designed both by and for users and make delivery of services easier. So then, the reason for introducing a computer system must be clearly acceptable, its operation must be congruent with the way service is delivered and the objectives of the part of the organisation into which it fits clearly understood. Implementation will be the less painful for this very difficult and traumatic analysis.

## RECENT DEVELOPMENTS IN COMPUTER HARDWARE

### R. K. Burdge

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In recent years advances in computer hardware have led to smaller, more robust and more reliable systems. A comparable machine that would have occupied a whole room, complete with air-conditioning and "clean mains supply", can now be accommodated on the office desk. The smaller machines or personal computers can be linked together either locally, within a building, or connected to similar or larger minicomputers on other sites, using communications equipment which is relatively cheap to install. These connections or networks allow the power and information to be distributed among the users, rather than being held centrally.

Instead of keyboards and visual display units, several alternative means of entering information are now widely available: mouse, bar-code reader, hand-held data collection unit, optical character reader and touch screen These devices used with modern software, made available by the increased memory in the machines, have led to systems that are easier to learn and use

## PROSPECTIVE AND RETROSPECTIVE DATA SEARCHES

### Hylton B. Meire

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The dream of every academically minded radiologist has long been to have the ability to recall from the departmental files all cases which show a particular radiographic sign or with a particular diagnosis. Manual filing systems used in a busy department do not permit any form of retrospective search. Prospective manual recording of interesting cases is time consuming and requires much space and dedication. When data from the radiology department are stored on computer, the prospective recording of interesting cases is made much quicker and easier by use of keywords or diagnostic codes.

Unpremeditated retrospective searches of the computer files are now becoming a possibility. Recent software developments now permit searching for words or phrases in free-narrative radiographic reports stored on the computer as well as a host of structured searches of the management data

Examples of prospective and retrospective searches are demonstrated and the relative advantages and dangers are discussed.

## MANAGEMENT BENEFITS OF THE RADIOLOGY COMPUTER

### R. M. Atkinson

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The talk is in three stages. The initial stage is a brief description of the radiology system at the Norfolk and Norwich Hospital which has been on-line since 1978. The cost of the equipment and the software is mentioned. The middle section deals with forthcoming developments to the software, *e g* · special costing and management budgeting using the existing software and a spread-sheet program. The last section is a discussion of future management and personnel programmes which are thought to be desirable and achievable, including leave and room rotas, appraisal diaries and automatic ordering and stock control programmes

## PITFALLS AND PROBLEMS WITH A COMPUTER X-RAY SYSTEM

### R. A. Owen

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The paper deals briefly with the problems and pitfalls that a newcomer to the X-ray computer field is likely to encounter. The type of computer options required are initially considered and from there the capacity requirements of the computer system are evaluated Proper training of the office personnel is mentioned together with the need for the software programmer to be "on site" for at least 2–3 weeks, when most software errors and corruptions are likely to appear and when operator errors can be identified and corrected

The importance of defining the exact specifications and performance requirements, especially response times, at all terminals under most adverse circumstances is discussed

Adequacy of the computer processing unit and its financial implications are highlighted. Some degree of redundancy in the hardware is advised and the installation of one rapid printer is advocated.

Tape back-up procedures, their duration and timing are considered along with the necessity for regular checking of record and report files and compression procedures, undertaken as and when required. The provision of a software warranty with proper and binding maintenance contracts is also discussed.

## Magnetic Resonance Imaging and Spectroscopy

**Chairman: Dr M. Smith**

Investigation of the distinctions between flow and susceptibility effects in magnetic resonance imaging, by I. R. Young, G M Bydder, A. G. Collins and S Khenia

Potential effects of susceptibility variations in pathological tissue on the quality of spectroscopic studies, by I R Young, I J. Cox, G M. Bydder, A. S Hall, D G. Gadian and B. D Ross

Localised phosphorus-31 spectroscopy *in vivo* using phase encoding nuclear magnetic resonance techniques, by D R Bailes, D J. Bryant, G M. Bydder, H A. Case, A. G. Collins, I J. Cox, R. R. Harman, A. S. Hall, S Khenia, P. McArthur, B. D Ross and I. R Young

PIMSS: a correction for muscle contamination in phosphorus-31 nuclear magnetic resonance spectroscopy using proton images and a phosphorus sensitivity image, by M. O Leach, V R. McCready, A. J. Hind, J. C. Sharp and D Collins

Measurement of modulation transfer function of magnetic resonance scanners, by R. A. Lerski, M. Fitzpatrick, D W. McRobbie, J L. Williams and W. Howarth

Posters.

Measurement of $T_1$ using the multiple inversion-recovery sequence, by I. R. Young, G. M. Bydder, A. G Collins and A S Hall

The variation of signal contrast and contrast-to-noise ratio in nuclear magnetic resonance fast imaging sequences, by M. O Leach, A J. Hind and P A. Gowland

Eddy currents in magnetic resonance imaging, by I. D Wilkinson, R. A. Lerski and D. W. McRobbie

### INVESTIGATION OF THE DISTINCTIONS BETWEEN FLOW AND SUSCEPTIBILITY EFFECTS IN MAGNETIC RESONANCE IMAGING

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The possibility that the phase changes ascribed to susceptibility variations (Cox et al, 1986) are in fact wholly or partly due to flowing blood is considered. Both coherent flow and susceptibility changes result in changes in the phases of voxels in the types of images which create the maps used to demonstrate the effects of haemoglobin degradation products. There has, however, been some discussion of the relative importance of the two effects, and it is desirable to resolve the uncertainty in order to predict the results of spectroscopic tests Phase maps are formed as the difference between the phase contributions of the voxels of two images, both partial saturation, but with data acquisition delayed in one relative to the other The images also contain errors due to main-field inhomogeneity, which it is desirable to correct Flow sensitisation can be introduced into the images using additional gradients, as in conventional flow measurement (Moran, 1982, Bryant et al, 1984). It is possible to achieve full-scale sensitivities of the order of 2–3 mm/s. Flow effects are frequently detected in phase maps designed to map suceptibility, but do not explain more than a fraction of the changes seen Flow effects are also seen in regions well away from the lesion being studied, which indicates the presence of slow flow through the normal brain.

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### POTENTIAL EFFECTS OF SUSCEPTIBILITY VARIATIONS IN PATHOLOGICAL TISSUE ON THE QUALITY OF SPECTROSCOPIC STUDIES

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The technique of susceptibility mapping, by determining phase changes between two free induction decay images, in one of which data acquisition is substantially delayed relative to the other, has been described elsewhere (Cox et al, 1986). The method has been used in various cases, particularly of tumours of different type and location and in a variety of cases of haemorrhage, including lesions arising from trauma The data from examination of over 100 patients were evaluated. Results show that when there has been significant bleeding, susceptibility effects of 0 4–1 ppm are regularly found In the case of tumours, no significant effect is found in around one third of cases, 0–0.2 ppm is found in another third and 0 2–1 ppm in the remainder. The effects found are enough to have a significant impact on $^1$H spectroscopy and are sufficient to cause significant potential errors in $^{31}$P analysis. Effects include loss of resolution, errors in chemical-shift results, splitting of lines, and difficulties in suppression of the water peak in hydrogen spectroscopy

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## LOCALISED PHOSPHORUS-31 SPECTROSCOPY *IN VIVO* USING PHASE ENCODING NUCLEAR MAGNETIC RESONANCE TECHNIQUES

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We have used a phase encode method (Kumar et al, 1975) to yield spatially resolved $^{31}$P spectra of normal and pathological human tissue *in vivo*. The spectral resolution we have achieved is considerably improved over previously published results (Hazelgrove et al, 1983; Bottomley et al, 1984), allowing us to analyse the nature of metabolism within a tissue in more detail. Spectra were obtained from a Picker research 1.6 T system. A saddle-shaped transmit coil and double-tuned surface coil were used Phosphorus spectra have been obtained from the sensitive volume of the receive coil and from 1 cm slices within the volume. The phase encoding technique was validated using phantoms and confirmed in volunteers. Its potential is illustrated by reference to a number of case studies: we demonstrate novel metabolism in the normal human liver, concentrations of adenosine triphosphate (ATP), inorganic phosphate (Pi), phosphodiester and phosphomonoester are defined, and the detection of pyridine nucleotides is discussed. A spectral resolution of less than 0.3 ppm is routinely obtained, enabling the J-couplings of ATP to be observed This method is used to define abnormalities in liver metabolism by $^{31}$P magnetic resonance spectroscopy. The only abnormality illustrated in the whole volume spectrum of a surface glioma is an increase in Pi concentration. However, the spatially resolved spectra show evidence of heterogeneous metabolism within the tumour We have exploited the technique to spatially map the response of limb-tumour metabolism to chemotherapy, which allows changes in the tumour volume to be accounted.

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## PIMSS: A CORRECTION FOR MUSCLE CONTAMINATION IN PHOSPHORUS-31 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY USING PROTON IMAGES AND A PHOSPHORUS SENSITIVITY IMAGE

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Surface-coil spectroscopy usually provides sufficient localisation for studies of muscle metabolism by $^{31}$P nuclear magnetic resonance spectroscopy. The study of $^{31}$P spectra derived solely from tumour *in vivo* often requires better localisation than can be achieved with a surface coil. Because of the irregular shape of many tumours and the close proximity of muscle or other tissue, surface coil methods, even when combined with spatially localised techniques such as DRESS, often produce spectra which include a contribution from tissues outside the tumour In the large majority of the tumours that we have studied, this has been the case. Phosphorus image muscle-subtracted spectroscopy (PIMSS) is a method of correcting for this muscle contamination that we have developed and are currently evaluating. The spatial sensitivity response of the surface coil at the appropriate transmitter power is obtained by producing a set of $^{31}$P images using an appropriate solution. The image is obtained in a fixed geometry with respect to the coil, using a gradient echo technique with gradients set to give the correct spatial distribution of signal. Before making the spectroscopic measurement in the patient, a set of $T_2$-weighted proton images of the region of interest are acquired using the body coil These have the same slice width as the $^{31}$P images and allow a water-containing marker in the surface coil to be visualised so that the relationship of the coil to tissue regions is accurately known. The $^{31}$P spectroscopic measurement then proceeds after shimming By identifying regions of muscle and tumour on the proton image, and transferring these data to the calibration image in each slice, the proportionate response from muscle can be assessed. If a spectrum derived from muscle alone, with the same coil, again corrected for coil response, is obtained, the contribution to each peak from muscle can be assessed. The muscle signal should ideally be derived from anatomically similar muscle close to the tumour site. It is important that relaxation effects are taken into account at each stage, either by allowing complete relaxation, or by using a suitable correction factor. The possibility of using a proton image for coil calibration, obtained with a double-tuned surface coil, is evaluated. It may prove possible to develop a method of assessing the muscle component on a pixel-by-pixel basis, to allow areas of infiltration to be corrected for. The method can be combined with methods of spatial localisation for greater accuracy

## MEASUREMENT OF MODULATION TRANSFER FUNCTION OF MAGNETIC RESONANCE SCANNERS

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The method of Judy (1976) has been used to investigate the modulation transfer function (MTF) of magnetic resonance scanners. A slightly angled wedge, which may be oriented in either the horizontal or vertical direction so as to correspond to the phase- or frequency-encoding direction, has been used to derive the MTF in six commercial imaging systems. It has been found that significant differences exist in the phase and frequency directions of most equipment and, further, that resolution varies considerably from scanner to scanner. Reasons for this variation between scanners may include inadequate eddy current correction and the use of gradients too small to counteract the main field inhomogeneity totally.

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## MEASUREMENT OF $T_1$ USING THE MULTIPLE INVERSION-RECOVERY SEQUENCE

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The demonstration of the relative efficiency of the multiple inversion-recovery sequence in the measurement of $T_1$ is considered. In the multiple inversion-recovery sequence, substantial recovery of the magnetisation is followed by an inverting (180°) pulse, with subsequent interrogation of the magnetisation by a series of pulses all having angles of significantly less than 90°, with the exception of the last one. Typically, four read-out radiofrequency pulses are used Adjustment of the relative magnitude of the pulses in a set can be used to characterise the resulting data. For example, they can be adjusted so as to obtain images with apparently constant contrast, or set so that one or two very good images are obtained for clinical purposes, although the other images in the set are poorer. To determine $T_1$, the sequence is designed so that the signal from any tissue from which a measurement is required is negative in the first image, and that the signal from at least one of the later images is positive. The measurement is made by determining the time at which the signals from any tissue are zero, by plotting the amplitudes of the signals from the images Comparison of results obtained with the multiple inversion-recovery sequence and those obtained using conventional inversion-recovery and long time-to-repeat partial saturation suggests the former method is reasonably accurate. Multiple inversion-recovery, for obtaining $T_1$ values, is relatively fast compared with other, more usual techniques.

## THE VARIATION OF SIGNAL, CONTRAST AND CONTRAST-TO-NOISE RATIO IN NUCLEAR MAGNETIC RESONANCE FAST IMAGING SEQUENCES

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Fast imaging techniques provide the possibility of obtaining diagnostic images in times short compared with conventional nuclear magnetic resonance imaging techniques. They may also allow respiratory artefacts to be reduced by the use of breath-holding techniques and for an increased number of slices to be obtained or studies to be carried out. The techniques we have available (FLASH and FISP) allow the pulse angle as well as the repetition time to be varied to alter the contrast between tissues and the signal. This results in increased complexity in determining the optimum sequence for clinical studies. We have performed a series of studies, using primarily gadolinium-doped solutions and gels, to investigate the changes in contrast-to-noise ratio and signal level with pulse sequence parameters. The measurements indicate that signal increases with repetition time and increases with pulse angle, except at short repetition times, where short pulse angles give enhanced signal The behaviour is complex The results of these measurements are presented in comparison with conventional sequences and their implications, in terms of information per unit time, are discussed.

## EDDY CURRENTS IN MAGNETIC RESONANCE IMAGING

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In magnetic resonance imaging, eddy currents (resistive or superconducting), are produced in the metallic structure of the magnet, during the application or removal of the imaging gradients. Generally the rise time of the gradients is kept short to minimise the delay until data collection, and although the amplitude of the gradients is quite low (around 5 $\mathrm{mTm}^{-1}$), the rate of change of the gradient field may approach 10 $\mathrm{Ts}^{-1}$. In fast imaging techniques (particularly echo-planar) these eddy currents are particularly active. The role of eddy currents as a perturbing influence, distorting the nuclear magnetic resonance signal, has only very recently started to receive attention in the literature although all manufacturers have developed their own methods of correction These are commonly based on adjusting the gradient waveforms to compensate for the presence of the eddy currents. These corrections must be determined experimentally and may be different for every differently arranged gradient scheme. Experiments have been performed both in a conventional resistive imaging system and an experimental test rig to quantify the severity of the eddy current problem and the variation of its effect over the field of view. The effectiveness of various correction schemes has been assessed, again as a function of position, since this may lead to resolution changes over the field of view.

*Proceedings of The British Institute of Radiology*

## Clinical: Genito-Urinary

**Chairman: Professor E. Rhys Davies**

Pre-operative radiological assessment of prostatic size. What are the roles of computed tomography and urethral pressure profilometry? By C. R. Chapple, D. Rickards, E J. G Milroy and R. T Turner-Warwick
Transrectal ultrasound in the diagnosis of inflammatory prostatic disease, by S Carter, A Doble, N. Thin, D. Rickards, W Harris, R. Witherow and N. O'Donoghue
Pelvic fracture, urethral stricture . . The significance of an open bladder neck, by S. Jones, J. Goligher, R. Turner-Warwick and D. Rickards
A comparison of barium double-contrast cystography and transabdominal ultrasound in the diagnosis of bladder tumours, by J. R Harding and G. J. Griffiths
Magnetic resonance imaging in bladder carcinoma, by J. P R. Jenkins, R. J. Johnson, R. J. Barnard, Y. Watson and I. Isherwood
The appearances on magnetic resonance imaging of persistent trophoblastic tumours and their role in management, by M. G. Long, A. W. L. Leung, J. E. Boultbee and K D. Bagshawe
The role of magnetic resonance imaging in the evaluation of endometriosis, by B. S Worthington, M. Powell and E M Symonds
Diagnosis and grading of chronic pancreatitis by morphological criteria derived by ultrasonography and pancreatography, by S. N. Jones, W R. Lees and R. A. Frost
Does arteriography contribute towards the surgical treatment of pancreatic disorders? By G. V. N. Appleton, N. Bathurst, R. C. N Williamson and J. Virjee
Per-nasal catheters for common-duct stones, by J. McGregor, D. F. Martin, M. E. Lambert and D. E. F. Tweedle
von Hippel Lindau disease: the problems of a screening programme, by P. A Gaines and C M. Jennings

### PRE-OPERATIVE RADIOLOGICAL ASSESSMENT OF PROSTATIC SIZE. WHAT ARE THE ROLES OF COMPUTED TOMOGRAPHY AND URETHRAL PRESSURE PROFILOMETRY?

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Benign prostatic hyperplasia is a common urological problem and is an important cause of morbidity with advancing age. Despite the research which has been carried out on this condition, its natural history is unpredictable. Not only is clinical assessment of prostatic size inaccurate, but also prostatic bulk may bear little relationship to the degree of obstruction and the subsequent incidence of urinary retention. Urodynamic investigation by means of videocystometry is now well established as an accurate and sensitive diagnostic technique for the detailed assessment of patients believed to have prostate-mediated bladder outlet obstruction Nevertheless, cases remain where standard urodynamic investigation produces equivocal results and where newer investigative techniques could be of additional value This study reviews a series of 21 consecutive patients who underwent videocystometry, urethral pressure profilometry and computed tomography (CT) of the prostate, before prostatectomy The urethral pressure profilometry utilised a standard fluid-flow technique and CT was carried out on a Siemens Somatom D. R. H machine, allowing calculation of prostatic volume and intraprostatic urethral length. The routine computer-aided videocystogram technique in use in our department is described

Estimation of intraprostatic urethral length by CT correlated closely with endoscopic operative measurements; the estimated prostatic volume bore little relationship to the quantity of prostatic tissue resected by the surgeon. Urethral pressure profilometry, although providing detailed information regarding the distribution of intraprostatic urethral pressure, is inaccurate as a measure of either prostatic bulk or urethral length and hence is of limited clinical value The implications of these findings and of our experience using videocystometry, for the routine investigation of patients with prostatic outflow obstruction in the district general hospital, are discussed.

### TRANSRECTAL ULTRASOUND IN THE DIAGNOSIS OF INFLAMMATORY PROSTATIC DISEASE

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Transrectal ultrasound is well established as a method of imaging the prostate for the diagnosis and staging of malignant disease. Little attention has been paid to its application to investigation of the benign diseases of the prostate Previous studies of young men's prostates have shown that the intraglandular anatomy can be well demonstrated Using a Bruel and Kjaer 1846 machine we have studied 63 patients with symptoms suggestive of chronic prostatitis and compared the transrectal ultrasound findings with those of conventional microbiological analysis. Abnormal echo densities in the peri-urethral region, subcapsular echo-free zones and peripheral diffuse changes involving the outer gland and capsule were detected significantly more frequently in patients with positive indications of prostatic inflammation. There was a distinct difference in the pattern of symptoms of those with central and peripheral changes. In 30 cases where investigations suggested the diagnosis of prostatodynia the above abnormalities were exceptionally infrequent. We conclude that this technique is a valuable adjunct to clinical and microbiological investigation of prostatic inflammatory symptoms and may cast light on the origin of haemospermia and some cases of male infertility

### PELVIC FRACTURE, URETHRAL STRICTURE . . . THE SIGNIFICANCE OF AN OPEN BLADDER NECK

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In approximately 10% of closed pelvic fracture injuries, urethral damage occurs. In the majority the end result is a short subprostatic stricture with minimal surrounding peri-urethral haematoma fibrosis. In a few, however, there is an extensive dislocation urethral defect with a marked retropubic haematoma and subsequent fibrosis Such injuries destroy the competence of the distal sphincter mechanism, the function of which cannot be reconstructed at surgery. Urinary continence therefore depends upon the bladder neck proximal sphincter mechanism following urethral reconstruction. Before surgery, the radiologist's role is to image the site and extent of the urethral defect. Cystography through a suprapubic catheter invariably demonstrates a wide open bladder neck at rest and contrast medium fills the posterior urethra up to the site of the defect. The distal extent of the defect is demonstrated by retrograde urethrography. The appearance of an open bladder neck is not due to sphincter damage, but to peri-urethral fibrosis holding the bladder neck open. To confirm this, 10 patients with closed pelvic fracture injuries had computed tomography (CT) of the inferior hemipelvis performed pre-operatively to assess the extent of peri-urethral soft tissue Surgery excises the fibrosis, releasing the bladder neck, and the urethra is reconstructed Subsequent recurrent fibrosis is prevented by a peri-urethral omental wrap, which was again demonstrated by CT In conclusion, a wide open bladder neck at cystography is not indicative of incompetence of the patient's only remaining sphincter mechanism, but merely reflects pelvic fibrosis following trauma.

## A COMPARISON OF BARIUM DOUBLE-CONTRAST CYSTOGRAPHY AND TRANSABDOMINAL ULTRASOUND IN THE DIAGNOSIS OF BLADDER TUMOURS

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A previous study of barium double-contrast cystography in 50 patients has shown the technique to be highly sensitive and specific in the detection of tumours as small as several millimetres in diameter, to give pre-cystoscopic information of exact site, size, shape and number of tumours and to demonstrate clearly whether they are polypoid or not. It has been particularly helpful in patients unsuitable for cystoscopy and for looking at areas inaccessible to cystoscopy, such as within narrow-necked bladder diverticula. The technique does, however, require bladder catheterisation with instillation of sterile barium and carbon dioxide, and radiological examination

Transabdominal ultrasound of the bladder has the avantages of being non-invasive, avoiding X-ray exposure, and allowing visualisation of extravesical structures, and should detect most tumours, though very small lesions may be missed. A trial has therefore been undertaken comparing barium double-contrast cystography with transabdominal bladder ultrasound, each study being conducted independently by a separate operator without knowledge of the result of the other investigation, but with the same clinical information and results of other investigations such as intravenous urography, urine cytology, etc, being available to both The results of the two techniques have been compared and correlated with cystoscopic and histological findings

Barium double-contrast cystography has been shown to be superior in the detection of small lesions and demonstration of intravesical morphology of bladder tumours, whereas ultrasound allows staging by assessment of invasion of the bladder wall and extension outside the bladder, and also detects extravesical pathology, such as ureteric dilatation secondary to tumour obstruction or incidental pelvic masses or cysts The two techniques are therefore complementary rather than competitive, each having specific advantages in providing different information Most patients with suspected bladder tumours in Newport now have both investigations

## MAGNETIC RESONANCE IMAGING IN BLADDER CARCINOMA

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Previous studies (Fisher et al, 1985; Amendola et al, 1986) have shown that magnetic resonance imaging (MRI), compared with computed tomography (CT), has been more accurate in the staging of bladder carcinoma. A major limitation of both techniques, however, has been their inability to identify accurately the depth of tumour penetration into the bladder wall to permit appropriate treatment planning To address this problem a study has been established to optimise imaging planes and pulse sequences and to correlate MRI findings with pathological staging This report presents the preliminary observations

Twenty patients with bladder carcinoma, established by cystectomy or cystoscopy and examination under anaesthesia, have been examined with a Picker International superconducting magnet system operating at 0 26 T. Following an initial sagittal pilot scan, a contiguous 16-image $T_1$-weighted (SE 1100/26) coronal multiset was performed Imaging planes were then selected, depending on the site of the tumour, and a variety of $T_2$-weighted sequences (TR 1500–2000/TE 60–120) and a free induction decay (FID) sequence (TR 500) were utilised From the initial coronal $T_1$-weighted images, the site of the tumour, including its exophytic component, together with any perivesical spread and pelvic lymph-node enlargement, were identified. Images obtained in the transverse plane provided sufficient information on extent of tumour confined to the anterior, posterior or lateral walls, together with involvement of the seminal vesicles. Images in the sagittal or coronal planes were, however, required to determine the full extent of tumours involving the dome or base of the bladder. Sagittal images were necessary to assess involvement of the prostate, rectum or vagina Heavily $T_2$-weighted sequences showed the greatest contrast between tumour and bladder wall, while the FID sequence, which provides edge enhancement, was useful in defining the boundary between the bladder wall and perivesical fat. The preliminary results suggest that, with careful technique to optimise image planes and pulse sequences MRI could have an increasingly important role in the management of bladder carcinoma.

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## THE APPEARANCES ON MAGNETIC RESONANCE IMAGING OF PERSISTENT TROPHOBLASTIC TUMOURS AND THEIR ROLE IN MANAGEMENT

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Eleven patients requiring treatment for invasive mole and choriocarcinoma have been studied using magnetic resonance imaging (MRI) in order to determine the appearance of these tumours within the uterus. The findings are compared with those of a corresponding ultrasound scan and a sensible role for the use of MRI in these diseases is presented. These tumours of trophoblastic origin have an incidence of approximately 1 in 15 000 pregnancies and the advent of cytotoxic chemotherapy has significantly reduced their fatality rate. The type of chemotherapeutic regime chosen depends on the expected risk of developing drug resistance. This is calculated from several clinical parameters, including the size of the uterine tumour, immediately before therapy.

We found that the uterine size or appearance was abnormal in eight patients using MRI and in seven using ultrasound. Magnetic resonance imaging clearly demonstrated tumour in all patients with a raised ultrasonic uterine volume or abnormal echo pattern. It also detected tumour in one of four patients with no ultrasonic abnormalities. The echo pattern changes were clear in only two patients and were otherwise much more subtle, whereas all the changes detected by MRI were well defined. It can be concluded that MRI may show tumour within the uterus where ultrasound has failed to do so and that it could play a useful role in the choice of optimum therapy for patients with persistent trophoblastic diseases with otherwise normal uterine findings.

We would like to thank both the Cancer Research Campaign and the Paul Strickland Scanner Appeal for their support with this project.

### DIAGNOSIS AND GRADING OF CHRONIC PANCREATITIS BY MORPHOLOGICAL CRITERIA DERIVED BY ULTRASONOGRAPHY AND PANCREATOGRAPHY

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The most commonly used tests in the diagnosis of chronic pancreatitis are ultrasonography (US), computed tomography and endoscopic retrograde pancreatography (ERP). Computed tomography is of value only in severe chronic pancreatitis. Both US and ERP are capable of showing ductal changes in mild forms of the disease, but comparison between the two has been difficult. At a meeting on the classification of pancreatitis in Cambridge in 1983, a set of morphological criteria and a descriptive terminology was established. We have applied this scheme to 85 patients with a firm clinical diagnosis of chronic pancreatitis. Twenty-seven patients were excluded from the study, four with a faulty clinical diagnosis and 23 with non-diagnostic pancreatograms. There was an exact classification into normal, equivocal, mild, moderate, or marked chronic pancreatitis in 50 out of 58 patients (86%) and an almost perfect correlation (± one grade) in 54 out of 58 (93%). There were four discrepancies: US missed focal pancreatitis in the tail, a small cavity in the uncinate process, and rare variant of chronic pancreatitis. One US scan was of poor diagnostic quality. Morphological grading by different techniques is feasible and use of this scheme can reduce diagnosis to a simple, specific set of rules.

### THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE EVALUATION OF ENDOMETRIOSIS

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Endometriosis is a common disorder of the reproductive system, mostly occurring in young nulliparous women and usually confined to the pelvis. The ovaries, rectovaginal pouch, parametria and posterior vaginal fornix are the commonest sites of implantation although the bladder and bowel may be implicated. A group of 30 patients with suspected endometriosis has been studied by ultrasound and magnetic resonance imaging (MRI) on a 0.15 T resistive system and the results compared with those at laparoscopy. Pathological tissue was associated with a different signal intensity on the same $T_1$- and $T_2$-weighted sequences, which presumably reflects its variable activity. The most valuable sequences for highlighting pelvic implants were a spin-echo sequence with a very long TE and a short tau inversion-recovery sequence in which $T_1$ and $T_2$ contrast are additive and the signal from pelvic fat is suppressed. In the detection of pelvic deposits they were correctly identified in nine patients and five were correctly declared free of disease; there was one false positive diagnosis and in two other patients tiny implants found at laparoscopy were not seen. Endometriotic cysts of the ovary were found in 13 patients and the signals associated with altered blood products within them allowed an estimate of their age. We conclude that MRI is superior to ultrasound in confirming the diagnosis when this is suspected clinically and is valuable for monitoring treatment whether by surgery or hormonal therapy. Laparoscopy is required, however, for staging to detect pin-point implants of disease beyond the range of imaging techniques.

### DOES ARTERIOGRAPHY CONTRIBUTE TOWARDS THE SURGICAL TREATMENT OF PANCREATIC DISORDERS?

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Selective visceral angiography should help to determine the nature and extent of pancreatic lesions and their suitability for resection. Between 1980 and 1986 coeliac and superior mesenteric angiograms have been obtained by transfemoral cannulation in 71 patients (mean age 50 years) considered for pancreatectomy, including 44 with malignancy and 28 with obstructive jaundice. Anomalous arterial anatomy was delineated in 20%, notably an aberrant origin of the right hepatic artery (14%). Among arterial changes observed in 41 patients (59%), increased or decreased vascularity and displacement were of limited diagnostic value, but encasement correctly predicted cancer in 17 of 19 cases and irresectability in nine of these. When present (17%), invasion or occlusion of the superior mesenteric or portal vein was more sensitive, indicating cancer in 11 of 12 cases and irresectability in 10 of these. Hepatic metastases were only detected in seven of 15 patients (47%). Overall angiography confirmed the diagnosis in 53%, localised the lesion in 69% (including three of five insulinomas) and correctly forecast irresectability in 65%; misleading data were obtained in four patients. There were no significant complications. Pancreatic angiography is a safe technique which contributes to the assessment of disease and the planning of operation, particularly when it shows arterial variation or venous obstruction. The results support its routine use before pancreatic resection.

### PER-NASAL CATHETERS FOR COMMON-DUCT STONES

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Fifty-nine patients with common-duct stones which could not be cleared immediately after endoscopic sphincterotomy had attempted endoscopic insertion of a per-nasal biliary catheter on a total of 65 occasions. The purpose of the catheter was to decompress and perfuse the bile ducts with clear fluids and subsequently to perform cholangiography in order to assess passage of stones There were 21 men and 38 women patients, mean age 74 7 (range 40–94) years. Thirty-six patients presented with obstructive jaundice, 10 with cholangitis, four with acute pancreatitis, five with biliary colic and four with retained stones after surgery. Insertion failed on four of 65 occasions. In three of these success was achieved at a later endoscopic retrograde cholangiopancreatography (ERCP). Fourteen tubes were dislodged from the common duct and two blocked. Eight patients had clear ducts after 4 days, another six had clear ducts between 5 days and 10 days and a further two had clear ducts after more than 11 days of per-nasal perfusion (a total of 16 clear ducts) Twenty-nine patients failed to clear their stones Of 43 patients in whom the procedure was not successful (failed insertion, dislodgement, blockage or failed clearance), 31 subsequently had their common-duct stones cleared at ERCP, 11 underwent biliary surgery and one patient died of unrelated causes Only two patients suffered possible complications, both having recurrent cholangitis while the per-nasal catheter was *in situ* It is concluded that although per-nasal biliary catheterisation is safe and may be useful for common-duct decompression and imaging, clearance of stones from the duct is successful in only a minority of cases

### VON HIPPEL LINDAU DISEASE: THE PROBLEMS OF A SCREENING PROGRAMME

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Von Hippel Lindau disease (VHL) is an uncommon familial disorder of autosomal dominant inheritance It was characterised initially by retinal angiomas and spinal and cerebral haemangioblastomas, but in recent years there has been wider recognition of its many abdominal manifestations, which include cysts of the liver, pancreas and kidneys Less commonly reported manifestations are multiple renal-cell carcinomas, phaechromocytomas and pancreatic apudomas. Once the diagnosis is established, screening becomes important: not only screening of the patient for possible early malignancies but also the family for the purposes of diagnosis and genetic counselling. We report the results of the radiological screening by ultrasound and computed tomography (CT) of the members of one such family.

The diagnosis is easily made in patients with multiple abdominal cysts. However, problems arise in patients with solitary hepatic, renal or pancreatic cysts The known prevalence of simple cysts in these organs must then be taken into consideration The diagnosis of renal-cell carcinomas, often bilateral or multifocal, and non-secreting pancreatic apudomas requires meticulous CT and ultrasound technique in the presence of multiple renal and pancreatic cysts In two of our cases with renal-cell carcinomas, histology revealed dysplastic, possibly pre-malignant cells lining several renal cysts. This suggests that renal cysts in VHL may be a pre-malignant condition. The problems of a radiological screening programme and a proposed protocol are discussed.

## Radiodiagnostic Physics and Instrumentation

**Chairman: Mr D. Gifford**

Measurement of effective dose equivalent in diagnostic radiology, by K Faulkner and R M Harrison

Acceptance testing and quality control in digital fluorography, by D J Hawkes, M. Fitzgerald, A Belli, G Tiller and A. Stewart

Assessment of film–screen combinations for mammography, by L. J. Furby and C. P. Lawinski

Recommended guidelines concerning the choice of projection in examinations of chest, abdomen, pelvis, sinus, cervical spine, lumbar spine, gallbladder, the gastrointestinal tract and the genito-urinary system, by I P Matthews, K D. Rogers and C J Roberts

Automated density measurements from lung computed tomography scans for the quantification of emphysema and fibrosis, by B. H Fromson and D. M. Denison

Dynamic "low-dose" three-dimensional computed tomography, by J E Gillespie, A Gholkar, C W Hart, D Mott and I Isherwood

### MEASUREMENT OF EFFECTIVE DOSE EQUIVALENT IN DIAGNOSTIC RADIOLOGY

K. Faulkner and R. M. Harrison

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A continuing problem in diagnostic radiology is the personnel monitoring of staff wearing a lead apron to determine the effective dose equivalent (EDE). The aim of this paper is to address this problem and give guidance on the monitoring of individuals The abdomen sections of a Rando phantom were irradiated by an overcouch X-ray tube to produce scattered radiation at a number of tube potentials Head and trunk sections of the Rando phantom, placed by the couchside, were loaded with lithium fluoride thermoluminescent dosemeter (TLD) chips at positions corresponding to a number of critical organs considered when calculating the EDE. In addition, film badge dosemeters were placed on the Rando phantom on the skin surface at the forehead, neck, chest and waist levels without a lead apron in position. Waist and chest film badge doses under different thicknesses of lead apron were calculated by applying a broad-beam transmission factor to these measurements The EDE was estimated for different combinations of tube potential and lead apron thickness Values for the EDE were then directly compared with the film badge dosimetry results.

### ACCEPTANCE TESTING AND QUALITY CONTROL IN DIGITAL FLUOROGRAPHY

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Currently accepted techniques for the assessment of imaging performance in radiology rely on subjective assessment of detail of known radiographic contrast in order to assess image noise and resolution. We have devised a procedure which uses the image data provided by digital fluorography to measure image noise. Estimates can be made of the separate contributions to the final image of both X-ray quantum noise and electronic noise. First the relationship between exposure to the image intensifier and the image grey level is found. After the subtraction of structured noise, the rate of change of image noise with exposure permits the derivation of the contribution of X-ray quantum noise. Noise in a dark region of the image provides an estimate of video and digitisation noise. This method has been verified by assessing imaging performance using either 8-bit or 10-bit analog-to-digital conversion. The modulation transfer function is derived from the system's response to bars of different spacings. This procedure has been used successfully in the acceptance testing of our digital fluorographic system (CGR DG300) The only requirements of this procedure are the calculation of the mean and standard deviation of the image grey levels over a selected region and the facility for the operator to manually select a range of X-ray exposures A simplified procedure has been developed for day-to-day quality control. The first six months' experience with this procedure is described and compared with our experiences of subjective procedures. The importance of routine quality control in digital fluorography is emphasised

### ASSESSMENT OF FILM–SCREEN COMBINATIONS FOR MAMMOGRAPHY

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The current interest in mammography has prompted manufacturers of X-ray imaging products to introduce new ranges of films and intensifying screens. By increasing the speed, these products aim to reduce the patient dose This study aims to ascertain to what extent the patient dose is reduced and whether this increased speed causes any loss in image quality Characteristic curves were plotted for each film–screen combination under test, from which the average gradient, the exposure latitude and the speed (relative to a selected standard combination) were calculated. The image quality and limiting resolution were evaluated by taking radiographs of a breast phantom and of a resolution grid Subsidiary experiments were done to evaluate the effect of change of thickness of attenuator, change of material used as attenuator, change of filtration of the beam, the effect of an antiscatter grid and change of tube voltage on the relative performance of these systems These results are presented to assist the user in the selection of films and intensifying screens for use in mammography.

### RECOMMENDED GUIDELINES CONCERNING THE CHOICE OF PROJECTION IN EXAMINATIONS OF CHEST, ABDOMEN, PELVIS, SINUS, CERVICAL SPINE, LUMBAR SPINE, GALLBLADDER, THE GASTROINTESTINAL TRACT AND THE GENITO-URINARY SYSTEM

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The exposure of very large numbers of people to low doses of diagnostic radiation may produce of the order of 300 extra cancers in the exposed population in the United Kingdom, according to current estimates. Under the auspices of the Royal College of Radiologists (RCR) we have conducted a survey of patient exposures in diagnostic X-ray departments throughout Wales between 1983 and 1986. This has demonstrated that there is a large variation in patient exposure between departments for each examination. The greater proportion of this variation is attributable to the variation between departments in the number of projections undertaken during a particular type of examination and the sizes of film used The interdepartmental variation observed in choice of projections for each examination is described and for each projection data are presented on the associated exposure The radiation exposure received by a patient during an examination is the sum of the exposures associated with each projection. Therefore choices of the minimum number of projections and the minimum film sizes (*i.e.* area of patient irradiated) which remain consistent with the desired clinical information will ensure that the radiation protection of patients is optimised. In this connection, recommendations are presented for each examination and their specific advantages are discussed It is estimated that approximately 80% of the substantial number of extra cancers arising from these examinations could be prevented by implementation of suitable guidelines aimed at reducing interdepartmental variations in patient exposure The development of guidelines will follow the sequence adopted by the RCR for pre-operative chest radiography and skull radiography

### AUTOMATED DENSITY MEASUREMENTS FROM LUNG COMPUTED TOMOGRAPHY SCANS FOR THE QUANTIFICATION OF EMPHYSEMA AND FIBROSIS

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Previous studies have shown the value of frequency distribution curves and spatial displays in the quantitative analysis of data from computed tomography (CT) of lung (Hayhurst et al, 1984, Denison et al, 1986). A semi-automated system that allows rapid determination of the distribution of the Hounsfield values within the lung has been developed and a graphical presentation of their spatial origin designed. The system uses the IAX image-processing language developed at Winchester and runs on an IBM 4381 mainframe connected to a Ramtek display system via an IBM Series 1 minicomputer. Scans of lungs are performed from apex to base in inspiration and expiration, using the Elscint 2002 whole-body scanner at the Brompton Hospital All images are recorded on tape and read by the IBM system, which displays up to 25 slices simultaneously in miniature. The operator indicates one point in each lung and trachea or main bronchus on each slice, and their boundaries are detected automatically Three-dimensional plots showing the slice-by-slice density distributions in each lung and each phase of respiration are generated and a graphical summary of whole-lung density distributions and gas and tissue volumes calculated. Three groups of people have been studied: normal subjects, patients with emphysema, and patients with fibrosing alveolitis. Transfer of the system to a smaller computer is being investigated to make it more widely available.

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## DYNAMIC "LOW-DOSE" THREE-DIMENSIONAL COMPUTED TOMOGRAPHY

J. E. Gillespie, A. Gholkar, C. W. Hart, *D. Mott and I. Isherwood

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Three-dimensional (3D) computed tomographic reformation has been used successfully as an adjunct to standard axial computed tomography (CT) in the evaluation of disorders affecting areas of complex anatomy. The basic requirements for high-quality 3D reformations are absence of patient movement during the examination and narrow-width trans-axial sections Speed of examination is an important factor in optimising image quality. All examinations were performed in the Department of Diagnostic Radiology on an IGE CT 9800 scanner Three-dimensional images were obtained using computer software program 3D98 For bone studies 80 mAs and for certain soft tissues 140 mAs are employed, both with a kV of 120. Three-dimensional examinations are now being performed routinely using a dynamic mode and such "low-exposure" factors The advantages of the "low-dose" technique are significant reduction in patient skin dose, faster examination (there is less time taken for tube cooling), and longer tube life. The main disadvantage is a reduction in signal-to-noise ratio. Nevertheless, the image quality obtained in 3D presentations has been sufficient to enable all bony abnormalities to be identified A similar "low-dose" technique is now being used for certain routine CT examinations Data from *in-vitro* and *in-vivo* dose-reduction studies are presented and clinical applications discussed.

*Proceedings of The British Institute of Radiology*

## Posters. Clinical: Neurology

**Chairman: Professor I. Isherwood**

Phosphorus-31 magnetic resonance spectroscopy in cerebral neoplasms: a combined study using magnetic resonance imaging and computed tomography, by I. J. Cox, D. B. Thomas, C Davies, I R Young, G M Bydder, D R. Bailes, D J Bryant, B. D Ross and S. Khenia

Gadolinium-DTPA in magnetic resonance imaging of intracranial mass lesions, by J P. Stack, R A Metcalfe, N. M Antoun, I Isherwood and J. P. R. Jenkins

Magnetic resonance imaging of craniopharyngiomas, by P Twining, B. S Worthington, R R Mawhinney and I. Holland

The role of magnetic resonance imaging in the assessment of arachnoid cysts, by T. Jaspan, M Wilson, B. S. Worthington, I Holland, J Punt, G Bydder and I. R. Young

Evaluation of tonsillar herniation in young hydrocephalic patients by low-field (0 08T) magnetic resonance imaging, by D M Kean, E Miller, J J. K Best and J F Shaw

Doppler ultrasound assessment of carotid artery stenosis: reassessment of the criteria for stenosis, by G G Hartnell, R Williams, R. N. Gibson and A. P Hemingway

Sources of error in the assessment of carotid artery disease by intravenous digital subtraction angiography and duplex Doppler Can they be avoided? By G G Hartnell, R Williams and A P Hemingway

### PHOSPHORUS-31 MAGNETIC RESONANCE SPECTROSCOPY IN CEREBRAL NEOPLASMS: A COMBINED STUDY USING MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY

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Energy metabolism in cerebral neoplasms can be monitored non-invasively using $^{31}$P magnetic resonance spectroscopy (MRS). Recently, conflicting reports of such studies in man (Oberhaensli et al, 1986) suggest either gross defects in energy metabolism or apparently small perturbations (Bottomley et al, 1984; Ng et al, 1986) To be of value, such information is best obtained in the context of existing imaging methods At the time of writing, 23 patients have been studied using $^{31}$P MRS, magnetic resonance imaging (MRI) and computed tomography (CT) to define the lesions before histological diagnosis A 1 6 T Picker research spectrometer has been used, with a saddle transmitter, and double-tuned surface receiver coil (of 6 cm diameter) In most studies we have used a method producing spectra from the whole volume excited by the coil (*c.* 100 g). In selected patients we have compared this result with that obtained by a spatially selective technique (details elsewhere in this Congress) Patients with all types of cerebral neoplasms represent the continuous clinical referrals of two neurosurgery units, and have not otherwise been specially selected for this study Imaging was on a 0.15 T Picker prototype imager at the Hammersmith Hospital. Successful spectroscopy was obtained in all but two patients (in one the tumour was seen to be beyond the range of the coil, in the other the signal-to-noise ratio was inadequate). Frankly abnormal spectra have been observed in only five patients, in each the abnormality was different. In 20% of the patient group, the sole abnormality was a subtle increase in intra-tumour inorganic phosphate (Pi) (expressed as a ratio of peak areas of Pi to adenosine triphosphate or phosphocreatine (PCr)) In the remainder, no abnormality was observed The pH, as measured by the chemical shift of Pi relative to PCr, was normal (7.10±0.06) except in one case in which an alkaline pH was measured. Imaging by MRI and CT yields the expected differences in volume and localisation of these cerebral tumours Susceptibility differences across tumours have been measured. In localised $^{31}$P spectra of selected cerebral neoplasms it has been possible to demonstrate heterogeneity of chemical composition across the tumour. We conclude that a combination of MRI, $^{31}$P MRS and CT yields additional information about cerebral neoplasms, and high-resolution $^{31}$P spectroscopy indicates near normal metabolism for this group of tumours The excess of Pi may indicate early necrosis or enhanced metabolic rate, properties which are compatible with the findings using positron emission tomography.

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### GADOLINIUM-DTPA IN MAGNETIC RESONANCE IMAGING OF INTRACRANIAL MASS LESIONS

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Eighty patients with a variety of intracranial diseases proven by computed tomography (42 primary brain tumours, six metastases, seven acoustic neuromas, 10 meningiomas, three arteriovenons malformations, two glomus jugulare, two colloid cysts, three infarctions, and one each of infection, neurofibroma, haemangiopericytoma, haemangioblastoma and multiple sclerosis) have undergone magnetic resonance imaging (MRI) using a variety of spin-echo (SE) sequences before and after injection of gadolinium-DTPA (dose 0 1 mmol/kg, patients 1–45 and 0.2 mmol/kg, patients 46–80). Signal-intensity time-profile studies over 50 min following injection of contrast medium, using a $T_1$-weighted SE sequence (TE 26/TR 560) were employed in an attempt to differentiate pathology All images were generated on a Picker International 0 26 T superconducting magnet system.

The $T_1$-weighted SE sequences demonstrated the greatest degree of signal increase in tumour tissue following injection of gadolinium-DTPA. The $T_2$-weighted SE sequences, although very sensitive in detecting intracranial disease, failed to discriminate oedema from underlying tumour, either before or after the administration of contrast medium Results demonstrate that gadolinium-DTPA is useful for shortening scan time, differentiating gross tumour from oedema in higher-grade gliomas and identifying small metastases, especially in the posterior fossa. It may also be of value in screening for acoustic neuromas and monitoring disease activity Time-profile studies have a role in the differentiation of certain pathological processes but in this study they failed to discriminate between tumour types. Meningiomas and acoustic neuromas enhanced most consistently, but exhibited similar characteristics over time. No side-effects from using gadolinium-DTPA were encountered

### MAGNETIC RESONANCE IMAGING OF CRANIOPHARYNGIOMAS

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The magnetic resonance findings in 13 cases of craniopharyngioma were reviewed and the results compared with those from computed tomography (CT) In five patients the tumours were associated with an increased signal intensity on both $T_1$- and $T_2$-weighted images which correlated with cysts containing lipid material. This feature was useful in differential diagnosis from other juxta-sellar tumours. Calcification, particularly when small in amount, was better demonstrated on CT. In the recognition of the full extent of the tumour in all three orthogonal planes magnetic resonance imaging proved superior to CT and the relationship to major vessels could also be appreciated without the need for contrast material The sagittal and coronal perspectives were especially useful in guiding the side and route of operative approach, in particular whether a transfrontal or transtemporal route was more appropriate.

### THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF ARACHNOID CYSTS

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Arachnoid cysts containing cerebrospinal fluid (CSF) occur in a number of intracranial sites. most commonly in the middle cranial fossa, overlying the hemispheres; in the posterior fossa, and in relation to the basal cisterns The main differential diagnosis is from parencephalic cyst, subdural collection, craniopharyngioma or cystic astrocytoma. Twenty patients with arachnoid cysts, the majority being in the middle cranial fossa, were examined by both computed tomography (CT) and magnetic resonance imaging (MRI) and the findings compared In the middle fossa cysts, MRI in the coronal plane was superior to CT in showing the mass effect on the temporal lobe. When complicated by a subdural collection after trauma a blood-stained collection from torn bridging veins could be distinguished from fluid deriving from the cyst. As with other pathology, the lack of bone artefact, the multiplanar facility and clear depiction of the brain surface allowed the extra-axial situation of the cysts to be clearly recognised The signal characteristics of cyst contents on the modulus variant of inversion-recovery and spin-echo sequences parallel those of CSF and allow a distinction from the protein-containing fluid of cystic neoplasms Better definition of the anatomical boundaries of the cysts facilitated the surgical approach to resection or marsupialisation into the CSF pathways

### EVALUATION OF TONSILLAR HERNIATION IN YOUNG HYDROCEPHALIC PATIENTS BY LOW-FIELD (0.08 T) MAGNETIC RESONANCE IMAGING

D. M. Kean, E. Miller, J. J. K. Best and J. F. Shaw

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Patients with spina bifida and myelomeningocele frequently also have other, associated abnormalities such as hydrocephalus and tonsillar herniation Thirty such patients have been examined by low-field magnetic resonance imaging (MRI) to evaluate the incidence and severity of tonsillar herniation. An attempt has also been made to correlate the degree of tonsillar herniation with the patients' clinical symptoms. Low-field MRI has been shown to be capable of demonstrating the anatomy of the foramen magnum very clearly and is far superior to other radiological techniques. The correlation between the degree of tonsillar herniation and clinical symptoms was relatively poor and several cases with clinical signs suggestive of severe tonsillar herniation had a normal MRI scan and vice versa. However, several patients with severe clinical signs were also seen who displayed significant tonsillar herniation. These patients benefited from posterior fossa decompression. It is therefore seen that MRI is useful in the assessment of this group of young patients with symptoms suggestive of tonsillar herniation to select those patients who would benefit from surgery

### DOPPLER ULTRASOUND ASSESSMENT OF CAROTID ARTERY STENOSIS: REASSESSMENT OF THE CRITERIA FOR STENOSIS

G. G. Hartnell, R. Williams, *R. N Gibson and A. P. Hemingway

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Duplex Doppler ultrasound has been used for several years as a non-invasive means of assessing the severity of extracranial carotid artery disease The current criteria used to correlate Doppler abnormalities with degrees of stenosis have a number of drawbacks In some reports the criteria are not clearly defined. In other reports the criteria are defined in terms of Doppler shift frequencies with no regard to the angle of insonation, which may introduce significant errors. Most reports have studied patients undergoing conventional carotid arteriography and are, therefore, applied to a population in which there are few normal cases and a high proportion of severe stenoses. We report the results of a prospective study comparing intravenous or intra-arterial digital subtraction angiography (DSA) with duplex Doppler in the assessment of carotid artery stenosis. We have compared the results of two widely used sets of Doppler criteria and reformulated these in terms of absolute changes in blood flow velocity. This reduces inaccuracies due to variations in angles of insonation Most of our patients were investigated by intravenous DSA and this safe method of angiography has allowed investigation of a larger proportion of patients with carotid arteries which were subsequently shown to be normal. The performances of the different Doppler criteria in our patients are compared with each other and with the results of DSA in over 80 patients (160 carotid bifurcations)

### SOURCES OF ERROR IN THE ASSESSMENT OF CAROTID ARTERY DISEASE BY INTRAVENOUS DIGITAL SUBTRACTION ANGIOGRAPHY AND DUPLEX DOPPLER. CAN THEY BE AVOIDED?

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Duplex Doppler ultrasound and intravenous digital subtraction angiography (DSA) are widely used in the assessment of extracranial carotid artery disease. Although these methods are safer than conventional angiography, there are many sources of error which reduce their accuracy. While some of these errors are apparent at the time of examination, others may not be detected and can have serious repercussions for patient management. We have examined a large number of patients using duplex Doppler ultrasound and intra-arterial or intravenous DSA. Several patients have also had surgery. We have analysed the cases where there has been a discrepancy between the Doppler, angiographic and, when applicable, surgical findings The causes of some of these sources of error have been identified and we suggest strategies for avoiding these errors. We discuss those features which can indicate that there may be erroneous results, particularly with duplex Doppler.

## Posters. Clinical: Cardiology

**Chairman: Dr B. C. Ogilvie**

Left ventricular quantitative analysis using digital subtraction angiography, by A. A. Mustafa, J. Peregrin, S. A. Saleh and M. S. Adili

Demonstration of aortic-root anatomy by intravenous digital subtraction angiography in infective endocarditis complicated by paravalvar abscess formation, by G J. Hunter, R. H Swanton and T Treasure

Preliminary findings of use of ultra-fast computed tomography to diagnose aortic valve stenosis, by R. M MacMillan, M. R Rees, F. J. Lumia and V. Maranhao

The effect of oral dipyridamole on the sensitivity and specificity of thallium-201 myocardial perfusion in patients suspected of suboptimal exercise, by S W. Smye, K. L Sheard and M R. Rees

The intermediate coronary artery, by M. Papouchado and R P. H Wilde

What do we mean by right coronary dominance? By M. Papouchado and R. P. H. Wilde

Coronary angioplasty in a regional centre clinical results and cost effectiveness over a 1-year period from a combined cardiology/radiology service, by N. Bishop, A F. Mackintosh and M. R. Rees

Evaluation of percutaneous transluminal coronary angioplasty with 17-(123-iodo)-heptadecanoic acid, by P. G. P. Stoddart, M. Papouchado, J. Vann Jones and R. P. H. Wilde

Evaluation of coronary bypass graft status and left ventricular function by ultra-fast computed tomography in patients with recurrent symptoms following surgery, by M. R Rees, R M. MacMillan and V. Maranhao

### LEFT VENTRICULAR QUANTITATIVE ANALYSIS USING DIGITAL SUBTRACTION ANGIOGRAPHY

Adel A. Mustafa, Jan Peregrin, Sanaa A. Saleh and Mahmoud S. Adili

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Digital subtraction angiography has recently been used for the assessment of cardiac physiology and function. Digital left ventriculograms were obtained in the 30° right anterior oblique position using a Digitron (Siemens) at the rate of 25 frames/s. Peak left ventricular (LV) ejection and filling rates were determined from the first derivative of the fitted TDC. Time to end-systole was determined from the occurrence of the first minimum of the TDC using Newton-Raphson iteration method. The slow filling duration of the LV diastolic function was obtained after identifying the slow filling start and end times Relevant LV volumes were obtained at these points as %SV These were slow and fast filling volumes, and the fast filling volume due to left atrium contraction. Results of LV function performance before and after surgery were compared using this method.

### DEMONSTRATION OF AORTIC-ROOT ANATOMY BY INTRAVENOUS DIGITAL SUBTRACTION ANGIOGRAPHY IN INFECTIVE ENDOCARDITIS COMPLICATED BY PARAVALVAR ABSCESS FORMATION

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The incidence of native valve infective endocarditis in the UK is in the region of 16 patients per million population per year. The overall mortality is 35%. Excluding patients who die before treatment can be started, the mortality in those adequately treated falls to 24%. Following insertion of a prosthetic heart valve the overall cumulative risk of developing either early or late infective endocarditis is in the region of 5%. This complication has a mortality of approximately 75% if medical treatment alone is employed, reducing to 50% if surgery and valve replacement are performed promptly. In either case, the development of a paravalvar infection, either in the aortic root or in the septum, substantially increases the mortality risk The onset of a conduction defect such as first degree heart block is good circumstantial evidence of aortic-root or septal abscess formation; under these circumstances prompt surgery is essential if the mortality rate is to be reduced The demonstration of the anatomy of an abscess is useful in planning such surgery, and current methods used include echocardiography, arterial catheterisation and computed tomography. The best data are produced by angiographic studies, the use of computed tomography is not an established technique for this purpose. Echocardiography is a valuable screening tool, but it is unable to provide anatomical information in a significant proportion of cases. Formal arterial catheterisation is not without complications and the introduction of a catheter near an abscess or friable vegetations is hazardous Hitherto, if first-class anatomical information has been absolutely essential pre-operatively, there has been no alternative but to accept the risk associated with direct arteriography on the basis that the benefits gained outweighed the possible complications. With the advent of intravenous digital subtraction angiography, it has been found to be possible to produce good-quality anatomical images of the aortic root and any abscess present, without the attendant possibility of dissemination of infected material or perforation. Even in sick patients images can be obtained which are of sufficient quality to enable appropriate surgery to be planned.

## PRELIMINARY FINDINGS FOR USE OF ULTRA-FAST COMPUTED TOMOGRAPHY TO DIAGNOSE AORTIC VALVE STENOSIS

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Eight patients, mean age 72 (range 64–80) years, five men and three women, with aortic valve stenosis documented by cardiac catheterisation, have been studied by ultra-fast computed tomography (CT) 1 day after catheterisation. Patients were scanned in the short-axis planar view for optimal visualisation of the aortic valve leaflets in a transverse slice through the leaflets A standard bolus of 42 ml of Renografin 76 was injected into the fasting patients through a median antecubital vein at a rate of 2 or 3 ml/s by a powered injector. Two consecutive eight-level r-wave triggered cine-mode scans (10 images/level) of the heart were acquired, starting above the aortic valve and continuing through the left ventricular apex. The scan slice through the aortic valve was identified and the end-systolic image visually analysed to determine whether a central orifice could be distinguished and area planimetered. Seven of the eight patients, all with calcified valves, had a central orifice visually detectable and area measured. The catheterisation-derived aortic valve areas were within 0.25 $cm^2$ of the CT-derived valve areas in all but one patient, who had significant aortic regurgitation Left ventricular mass was measured in the eight patients with aortic valve stenosis ($121.6 \pm 18.2$ $g/m^2$) and for a group of eight subjects with normal left ventricular function, no history of hypertension and normal electrocardiograms ($73.0 \pm 13.1$ $g/m^2$). A significant difference ($p < 0.0001$) was found for left ventricular mass between the aortic stenosis group and the normal group. The left ventricular mass for the normal group was within the range of normal for established left ventricular mass by cardiac catheterisation ($92 \pm 16$ $g/m^2$). We conclude that in selected cases of aortic valve stenosis, ultra-fast CT can provide a definitive diagnosis and assess severity of stenosis by direct measurement of valve orifice.

## THE EFFECT OF ORAL DIPYRIDAMOLE ON THE SENSITIVITY AND SPECIFICITY OF THALLIUM-201 MYOCARDIAL PERFUSION IN PATIENTS SUSPECTED OF SUBOPTIMAL EXERCISE

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Two groups of patients, matched for age, sex and severity of coronary artery disease, were studied retrospectively to compare the effect of oral dipyridamole on the sensitivity and specificity of thallium-201 myocardial perfusion imaging All patients with a history of myocardial infarction within the previous 6 weeks, cardiomyopathy and aortocoronary bypass grafting were excluded All patients underwent coronary arteriography within 6 months of the thallium investigation and had no significant change in symptoms between the angiogram and thallium test. Each group comprised 27 patients. Group 1 patients underwent a standard exercise regime before the acquisition of thallium-201 digital perfusion images in the anterior and 45° and 70° left anterior oblique positions This image sequence was then repeated after 4 h, without exercise Group 2 patients underwent a similar image acquisition sequence, but were given 300 mg/m dipyridamole orally 1 h before exercise. Patient's echocardiograms (ECGs) were monitored during exercise and all patients in both groups were selected on the basis that their heart rates failed to reach a set target (200 − age) and that no ischaemic changes in the ECG were noted Each thallium myocardial image was divided into three segments and the segmental activity scored as normal (0), mildly reduced (1), or severely reduced (2). Each segment was assigned to an arterial territory· left anterior descending (LAD), right coronary (RC) and circumflex (CX). Coronary arteriograms were scored using the following grades· 0 (<70% stenosis), 1 (70–90%), 2 (90–99%) and 3 (100%). Agreement between thallium and angiographic scores was assessed on a territorial basis for each group (Table I).

TABLE I

| | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|
| | LAD | RC | CX | LAD | RC | CX |
| Sensitivity (%) | 90 | 67 | 73 | 96 | 82 | 100 |
| Specificity (%) | 43 | 78 | 67 | 50 | 69 | 86 |

The significance of these results and the indications for the use of oral dipyridamole in this group of patients are discussed

## THE INTERMEDIATE CORONARY ARTERY

M. Papouchado and *R. P. H. Wilde

*Department of Cardiology and *Department of Radiodiagnosis, Bristol Royal Infirmary*

In a number of hearts the left main coronary artery forms a trifurcation. The importance of the middle branch, the intermediate coronary artery, is not well documented. Using the myocardial scoring system of Brandt et al (1977), we have analysed 1017 consecutive coronary arteriograms to ascertain the incidence, size and surface distribution of this vessel. Four hundred and twenty-one hearts (41.6%) had an intermediate coronary artery, of which 64 (15.2%) were judged to be insignificant in size. In the remaining 357 hearts the myocardial value showed a wide variation (Table I). The vessel was usually single (329 cases, 92%), but was double in 26 cases (7%) and treble in two (<1%). The myocardial region supplied by a significant intermediate vessel also showed wide variation The distribution was confined to the diagonal area in 112 cases (31.3%) and to the obtuse marginal area in 44 (12.3%) The vessel supplied portions of both the diagonal and the obtuse marginal areas in 158 cases (44.2%) and of both the obtuse marginal and inferior areas in nine (2.5%). In 34 cases (9%) the vessel supplied portions of all three regions In five cases the first septal branch arose from an intermediate vessel Fifteen cases had no significant diagonal branches from the left anterior descending artery, the diagonal region being supplied entirely by the intermediate coronary artery in 12 cases, the intermediate and a circumflex branch in two and entirely by circumflex branches in one. We conclude that a full arteriogram report should identify all vessel origins, including the presence or absence of the intermediate coronary artery· description of the left ventricular free wall branches alone is incomplete

## REFERENCE

Brandt, P. W T, Partridge, J B. & Wattie, W. J., 1977. Coronary arteriography; method of presentation of the arteriogram report and a scoring system *Clinical Radiology*, *28*, 361–365.

TABLE I

| Myocardial value (Brandt score) | No. of cases |
|---|---|
| 0.5/15 | 86 (20%) |
| 1/15 | 71 (17%) |
| 1.5/15 | 74 (17.5%) |
| 2/15 | 49 (11.6%) |
| 2.5/15 | 40 (9.7%) |
| >3/15 | 37 (8.7%) |

## WHAT DO WE MEAN BY RIGHT CORONARY DOMINANCE?

M. Papouchado and *R. P. H. Wilde

*Department of Cardiology and *Department of Radiodiagnosis, Bristol Royal Infirmary*

The arterial supply to the inferior left ventricular free wall and inferior septum is not uniform, but may be derived entirely from the right, entirely from the left or from both coronary arteries in varying reciprocal proportions There is very little available data concerning the relative contribution of each of these vessels Using the myocardial scoring system of Brandt et al (1977), we have analysed 1017 consecutive coronary arteriograms to identify the origins and relative sizes of the inferior surface branches. Seven hearts showed coronary-artery anomalies and are thus excluded. Defining coronary dominance as the artery which gives rise to the vessel or vessels in the posterior interventricular groove, 109 cases (10.7%) showed left and 872 (85.7%) showed right dominance. In 29 cases (2.9%) both right and left coronary arteries provided an inferior septal branch, so dominance was mixed Cases with right dominance could be subdivided according to the area of inferior left ventricular myocardium supplied. In 77 cases (7.6%) the right coronary artery supplied the posterior descending artery alone, the entire inferior surface supply coming from the left. In 142 cases (13.9%) the dominant right coronary artery supplied up to one third, in 227 (22.3%) between one and two thirds, and in 348 (34.2%) between two thirds and the whole of the inferior cardiac surface. Large branches from the right coronary artery passing beyond the inferior onto the obtuse marginal region were encountered in 78 cases (7.6%).

We conclude that the size and surface distribution of the right coronary artery are variable. Use of the term "right coronary dominance" does not adequately indicate the contribution this vessel makes to the blood supply of the left ventricle. The area of inferior left ventricular myocardium supplied by the right coronary artery, in addition to the inferior septum, should be defined.

## REFERENCE

Brandt, P. W. T, Partridge, J. B. & Wattie, W. J, 1977. Coronary arteriography, method of presentation of the arteriogram report and a scoring system. *Clinical Radiology*, *28*, 361–365

## CORONARY ANGIOPLASTY IN A REGIONAL CENTRE: CLINICAL RESULTS AND COST EFFECTIVENESS OVER A 1-YEAR PERIOD FROM A COMBINED CARDIOLOGY/RADIOLOGY SERVICE

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Eighty patients (20 women, 60 men, age range 35–75 (mean 54.5) years) underwent percutaneous transluminal coronary angioplasty (PTCA) at our centre from November 1985 to October 1986. The service was carried out by two experienced operators (a consultant radiologist and a consultant cardiologist). All patients had been investigated with a view to interventional treatment by either surgery or angioplasty. Sixty-one patients had single-vessel disease, 14 had double-vessel disease and five had triple-vessel disease Eighty-four per cent of patients (67) had good ventricular function, 12% moderate (10 patients) and 4% (three patients) poor ventricular function Distribution of lesions treated by angioplasty were: left anterior descending/diagonal, 51 (62%), right coronary, 18 (22%) and circumflex, 13 (16%). One patient received a bypass graft. Two patients had double-vessel angioplasty Primary angiographic success was achieved in 75% of all cases and 82% of stenotic lesions Four patients have developed recurrent stenosis. Of the angiographic "failures", four were from acute vessel occlusion and 11 from inability to cross the lesion In three patients the lesion was crossed but showed no improvement. No mortality was attributed to the procedure, but one patient died with pre-existing cardiogenic shock. Other complications were one false aneurysm of the femoral artery, one fracture of the catheter (requiring surgical removal), one transient atrial fibrillation, one cardiac arrest with balloon inflation (the patient recovered fully) and one transient diplopia. Hospital stay was 3–28 (mean 5.5) days In treatment of the 80 patients, 104 guide wires, 123 guide catheters and 114 balloon catheters were used An average cost for disposable equipment for each procedure was £730. The total average cost for PTCA was £1565 per patient compared with an average cost for coronary artery bypass grafting of £2529 per patient

## EVALUATION OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY WITH 17-(123-IODO)-HEPTADECANOIC ACID

P. G. P. Stoddart, *M. Papouchado, *J. Vann Jones and R. P. H. Wilde

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17-(123-iodo)-heptadecanoic acid (HDA) is used to investigate myocardial perfusion, its distribution being proportional to the coronary arterial supply. The clearance half-life of HDA is dependent on the metabolic status of the myocardium, being prolonged by ischaemia and accelerated by infarction. Ten patients with stable angina were investigated by coronary angiography and subsequent myocardial scanning with HDA. The HDA was injected in the last minute of symptom-limited exercise testing. Six patients were rescanned following percutaneous transluminal coronary angioplasty. The hearts were imaged from the apex, and the uptake and clearance half-life of HDA were assessed in four left ventricular regions (anterior, obtuse, inferior and septal). There were 32 myocardial regions which were supplied by a stenosed coronary artery, the uptake of HDA was visibly reduced in 21 of these regions. Defects were more common in regions supplied by the more severely stenosed arteries. Five of the angioplasties were clinically successful. In two patients the uptake of HDA distal to the dilated stenosis was restored to normal by the procedure. One patient suffered a myocardial infarct in consequence of the angioplasty, in this case a defect appeared in a previously normal region. The mean clearance half-life of HDA from the 16 regions with an arterial stenosis greater than 90% (35.69±41.25 min) was longer than the expected normal mean (18.85±3.35 min), but the difference is not statistically significant. There was no consistent change in the half-life in the myocardial regions whose arterial supply was affected by angioplasty. It is concluded that HDA may be used for the investigation of coronary disease by static imaging of the myocardium. However, the half-life cannot be measured with sufficient consistency for it to be of clinical value.

## EVALUATION OF CORONARY BYPASS GRAFT STATUS AND LEFT VENTRICULAR FUNCTION BY ULTRA-FAST COMPUTED TOMOGRAPHY IN PATIENTS WITH RECURRENT SYMPTOMS FOLLOWING SURGERY

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*Killingbeck Hospital, Leeds and *Deborah Heart and Lung Center, Brown Mills, New Jersey, USA*

From May, 1985, to July, 1986, 84 consecutive patients with recurrent chest pain 3 weeks to 10 years after coronary bypass surgery were studied by ultra-fast computed tomography (CT) to assess graft patency and ventricular function. Three studies were technically unsatisfactory. Three image sequences per patient were required to complete the examination (80 images/sequence). Each image sequence required the intravenous injection of 35 ml of contrast medium using a powered injector. The remaining 81 patients had 199 grafts placed at surgery (160 single vein, 23 sequential vein and 16 internal mammary). A graft was patent if seen on two or more levels and flow was confirmed by time–density curve analysis. A total of 160 grafts were seen by CT. One hundred and thirty-nine were patent, 29 were occluded (graft stump or graft seen but no flow) and 39 not seen were presumed to be occluded. Grafts were localised to major coronary artery territories (right, left and circumflex) in comparison to the surgical reports (98% accuracy). Localisation to subdivisions of these territories was 80% accurate. When studies were reviewed blind there was an increase in graft detection of 15% for the first 100 grafts and 8% for the final 99 grafts examined compared with the original reports, demonstrating a significant learning technique in study interpretation. Twenty-one of the 81 patients underwent selective graft catheterisation as well as CT. An accuracy of 93%, a sensitivity of 90% and a specificity of 93% were found for CT vs catheterisation. We also demonstrated a significant correlation ($r = 0.93$) for CT-derived ejection fraction compared with left ventriculography. We concluded that ultra-fast CT is a highly reliable technique for the follow-up of patients after bypass graft surgery.

## Posters. Clinical: Vascular

**Chairman: Dr A. L. Hugh**

Embolisation in the management of external carotid arteriovenous malformations, by A. P. Hemingway and D. J. Allison

Treatment of pulmonary arteriovenous malformations: experience with coil embolisation, by G. G. Hartnell, E. J. Smith and D. J. Allison

The management of giant systemic arteriovenous malformations, by A. P. Hemingway, E. J. Smith and D. J. Allison

Volume flow measurement with duplex scanning in femoropopliteal bypass grafts, by M. D. McShane, V. M. Gazzard, A. M. Cotton, K. N. Humphries and A. D. B. Chant

Limb blood flow measurement in peripheral vascular disease using a gamma camera, by A. Parkin, P. A. Wiggins, P. Vowden, D. Wilkinson, P. J. Robinson, M. C. P. Salter and R. C. Kester

Early experience with the Gunther inferior vena caval filter, by J. V. Hunter, D. Irving and J. Reidy

The appearance on computed tomography of the inferior thyroid veins, by A. Belli, C. Ingram, C. Heron and J. E. Husband

## EMBOLISATION IN THE MANAGEMENT OF EXTERNAL CAROTID ARTERIOVENOUS MALFORMATIONS

Anne P. Hemingway and *D. J. Allison

*Department of Diagnostic Radiology, Hammersmith Hospital and *Royal Postgraduate Medical School, Hammersmith Hospital, London*

Arteriovenous malformations in the external carotid artery territory present vascular and plastic surgeons with formidable management problems. Treatment may be necessary on cosmetic and/or medical grounds. The lesions can bleed in an uncontrollable fashion, cause symptoms of compression or obstruction of vital structures and, if very large, can cause high-output cardiac failure. Surgical treatment may involve attempted resection, which is hazardous owing to excessive blood loss and the proximity of neighbouring vital structures. Frequently all that is possible is the ligation of feeding vessels, which may effect a temporary reduction in size but in no way alters the natural progression of the lesions, and renders therapeutic embolisation impossible. Transcatheter therapeutic arterial embolisation has provided a valuable and successful alternative form of treatment. It does not completely cure the underlying abnormality but in most instances reduces the size and vascularity of the lesions along with their potential to bleed spontaneously. In some cases it may facilitate curative surgery. It has the added advantage that it leaves no scar and can be repeated as often as is necessary. All vascular procedures within the carotid territory carry risks. The most serious potential complications of embolisation include blindness, hemiplegia and even death. These fortunately rare complications must be weighed against the hazards of doing nothing at all or surgery, and must be discussed in detail with the patient. We present the results of 49 embolisation procedures in 27 patients with arteriovenous malformations in this region. The indications for embolisation, the agents used and the complications encountered are discussed.

## TREATMENT OF PULMONARY ARTERIOVENOUS MALFORMATIONS: EXPERIENCE WITH COIL EMBOLISATION

G. G. Hartnell, *E. J. Smith and D. J. Allison

*Departments of Diagnostic Radiology and *Surgery, Hammersmith Hospital, London*

Surgical treatment of pulmonary arteriovenous malformations (AVMs) is being replaced by percutaneous transcatheter embolisation techniques. Embolisation is safer, causes less damage to normal lung and can be used to treat multiple malformations which cannot be dealt with surgically. Most reports of embolisation of pulmonary AVMs refer to the use of detachable balloons. Although these are effective, safe balloons are very expensive and can be difficult to position satisfactorily. We describe our experience with the use of steel coils in the treatment of pulmonary AVMs.

Six patients with multiple pulmonary AVMs have been treated by steel-coil embolisation. This usually needs to be performed on several separate occasions to allow complete embolisation. In spite of this, patient acceptability is good and there is a low incidence of significant complications. Some patients have a very good result following embolisation of a few discrete AVMs and in these cases embolisation may be curative. Some patients have a large number of AVMs, some of which are too small and numerous for embolisation. In these cases the aim of embolisation is to reduce hypoxia and the risk of stroke, by embolising the larger lesions even though complete cure is impossible. Patient selection, the technique and the results of embolisation are discussed.

## THE MANAGEMENT OF GIANT SYSTEMIC ARTERIOVENOUS MALFORMATIONS

Anne P. Hemingway, *E. J. Smith and D. J. Allison

*Departments of Radiology and *Vascular Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, London*

Massive congenital systemic arteriovenous malformations present considerable management problems for clinicians. Their size, position and vascularity frequently make successful surgical resection impossible. If sited distally in a limb amputation can be offered; more centrally placed lesions have in the past been treated with radiotherapy and surgical ligation of feeding vessels. These forms of treatment produced only temporary relief of symptoms and often caused further disfigurement. The need for a successful, alternative method of treating these lesions is not based on cosmetic considerations alone. Large arteriovenous malformations behave in many respects as malignant tumours. Their growth gives rise to local symptoms of pain, swelling and distal ischaemia. They can erode bone, trivial trauma can give rise to life-threatening haemorrhage and the massive left-to-right shunts eventually give rise to high-output cardiac failure and sometimes death. Therapeutic arterial embolisation offers a relatively safe and effective means of controlling these lesions. A number of recent developments, including the introduction of non-ionic contrast agents, digital subtraction angiography and the production of numerous embolic materials, has made it possible for the interventional vascular radiologist to manage these previously untreatable lesions. We present the results of the procedure in the management of nine patients who have undergone a total of 26 embolisation procedures. The materials used, techniques employed and complications encountered are discussed.

## VOLUME FLOW MEASUREMENT WITH DUPLEX SCANNING IN FEMOROPOPLITEAL BYPASS GRAFTS

M. D. McShane, *V. M. Gazzard, *A. M. Cotton, *K. N. Humphries and A. D. B. Chant

*Departments of Vascular Surgery and *Medical Physics, Southampton General and Royal South Hants Hospitals, Southampton*

A study is in progress to evaluate the potential to quantify blood flow rates through lower limb grafts using duplex scanning. A postulated cause of graft failure is kinking during knee flexion leading to a reduction in flow rate and thrombosis. This study was designed to compare flow in the grafts with the leg extended and flexed to determine whether a noticeable reduction occurs. Validation studies were performed on a pulsatile flow rig over a range of flow rates and tube diameters, with reasonable correlation (0.81–0.99) with timed fluid collection. Thirty-five patients have been studied. Ten grafts above the knee showed no significant reduction in volume flow with knee flexion. Twenty-five patients with bypass grafts below the knee similarly showed no significant reduction in volume flow with the knee flexed to 90°. In individual cases significant changes in volume flow have been observed. Duplex scanning can be used to measure volume flow non-invasively. In patients with patent grafts preliminary results show that overall there is no significant reduction in flow with knee flexion.

## LIMB BLOOD FLOW MEASUREMENT IN PERIPHERAL VASCULAR DISEASE USING A GAMMA CAMERA

A. Parkin, P. A. Wiggins, *P. Vowden, *D. Wilkinson, †P. J. Robinson, *M. C. P. Salter and *R. C. Kester

*Departments of Medical Physics, *General Surgery and †Diagnostic Imaging, St James's University Hospital, Leeds*

A method for measuring limb blood flow using technetium-labelled red cells or human serum albumin has been developed. Subjects are positioned with legs and feet over a gamma camera with a large field of view, and pneumatic cuffs are inflated below the knees to isolate the blood in the lower limbs and to induce a hyperaemic response. The remaining blood pool is labelled with technetium. Blood flow is derived from the linear phases of time–activity curves generated for the legs following the release of the cuffs and by venous sampling of the equilibrium blood pool. Results for patients with claudication and arterial occlusions on translumbar aortography are (in units of mean flow per unit volume) claudicants (27 limbs), 3.3 ± 2.1 ml/100 ml/min, and normal controls (24 limbs), 15.6 ± 3.5 ml/100 ml/min. A tissue-equivalent phantom of a human leg connected to a peristaltic pump has been used to validate the technique and good agreement has been observed between measured flow rates and those calculated from time–activity curves ($r = 0.99$). Reproducibility established by repeated measurements on 34 limbs is high at both high and low flow rates ($r = 0.99$) An example of the use of the technique to monitor changes in blood flow following balloon angioplasty is presented

### EARLY EXPERIENCE WITH THE GÜNTHER INFERIOR VENA CAVAL FILTER

J. V. Hunter, D. Irving and J. Reidy

*X-ray Department, Guy's Hospital and Radiology Department, Lewisham Hospital, London*

Pulmonary embolism arising secondary to deep venous thrombosis still remains a significant cause of morbidity and mortality. Despite anticoagulant therapy and fibrinolysis there is a minority of patients who require some form of inferior vena caval interruption to prevent pulmonary thromboembolism. Currently the Greenfield filter is the device which has found most widespread clinical acceptance, with a final caval patency rate of 95% However, it needs a surgical venotomy, or considerable dilatation of the puncture site, for insertion because of its large delivery capsule. Furthermore, *in-vitro* work has suggested that eccentric placement of a Greenfield filter results in a marked reduction in its efficacy in preventing the passage of simulated clot Migration of the filter to the right heart has also been described. We report on the availability and early performance of a new filtration device which is more easily inserted under local anaesthesia using conventional percutaneous techniques. We have inserted 14 filters into 13 patients without mortality or significant morbidity. There has been symptomatic improvement in all patients. Long-term performance is being monitored by clinical assessment, ultrasonography and inferior vena cavography. Preliminary results of the follow-up investigations show no complications up to 1 year after filter placement. A full series of follow-up results is reported for our patients, with a review of other European experiences

### THE APPEARANCE ON COMPUTED TOMOGRAPHY OF THE INFERIOR THYROID VEINS

A. Belli, C. Ingram, C. Heron and J. E. Husband

*Department of Radiology, St George's Hospital, London*

The anatomy of the inferior thyroid veins is of importance radiologically because sampling of thyroid veins is an accurate method of localising hyperfunctioning parathyroid glands. The variations in anatomy demonstrated at parathyroid venous sampling are well described, but to our knowledge the appearances on computed tomography (CT) of inferior thyroid veins has not been reported. The inferior thyroid veins are frequently multiple and after ramifying in front of the trachea, they join inferiorly to form two main veins. These may enter the right and left innominate veins separately, but in 60% of cases they converge to form a single trunk which usually terminates in the left innominate. Eighty CT scans of the superior mediastinum were reviewed retrospectively All patients had Stage I testicular teratoma with CT appearances and clinical markers unchanged for more than 1 year. Consecutive scans demonstrated small structures identical to vessels seen in cross-section, lying in the expected position of the inferior thyroid veins. The number of veins seen on each section and the number of contiguous scans on which they could be identified were recorded for each patient Structures conforming to the inferior thyroid veins were seen on 73 scans and their linear nature confirmed by the fact that 85% were seen on more than one scan In 42% the lowest scans showed a smaller number of veins than the higher scans and in 77% only one vein was seen on the lowest scan, corresponding to the usual pattern of convergence. Although none of these patients required intravenous contrast medium, enhancement of similar structures has been observed in other patients The same structures were identified in a normal volunteer undergoing magnetic resonance imaging Three areas of low signal intensity, consistent with flowing blood, were seen and this was thought to confirm further their vascular nature.

## Mackenzie Davidson Memorial Lecture

### THE CLINICAL BIOLOGY OF TESTICULAR GERM-CELL TUMOURS

M. J. Peckham

*British Postgraduate Medical Federation, London*

The aetiology of testicular cancer is unknown, although it seems likely that factors which may determine the genesis of germ-cell malignancy operate many years before clinical presentation, in pregnancy or early childhood Thus, carcinoma *in situ* in the germinal epithelium may evolve into invasive malignancy over a protracted time course, in some cases decades Current knowledge of aetiological factors, including testicular maldescent, are reviewed and *in-situ* carcinoma discussed with particular reference to its potential relevance in management

The experience of the Testicular Tumour Unit at the Royal Marsden Hospital over 1975-85 is used to illustrate factors determining treatment outcome with radiotherapy and chemotherapy. On the basis of these observations the case for a management strategy based on a knowledge of prognostic factors is developed and the results of implementing such a policy presented The success of chemotherapy has led to the introduction of surveillance following orchidectomy for Stage I seminoma and teratoma of the testis. This policy, introduced in 1979, has shown that the surveillance strategy is feasible and effective. The identification of factors that predict relapse in Stage I disease permits the introduction of adjuvant chemotherapy for high-risk patients Three other important areas are discussed the phenomenon of tumour maturation, the effects of chemotherapy on spermatogenesis, including the monitoring of children fathered by successfully treated patients; and the psycho-social effects of diagnosis and management.

*Proceedings of The British Institute of Radiology*

# Nuclear Reactor Accidents: Preparedness and Medical Consequences. One-Day Seminar

Please note that the *British Journal of Radiology* will be publishing the full papers from this seminar later this year.

## Session I

**Chairman: Sir Donald Acheson**

Medical/radiobiological basis of radiation accident management, by C. C Lushbaugh, S A Fry and R. C. Ricks
Medical basis for the establishment of intervention levels, by J C Nénot
Clinical experience of reactor accident management, by E. Komarov and N M. Nadezhina. No abstract received
The role of NHS hospitals in the preparedness for nuclear reactor accidents, by P. Bourdillon No abstract received

### MEDICAL/RADIOBIOLOGICAL BASIS OF RADIATION ACCIDENT MANAGEMENT

C. C. Lushbaugh, S. A. Fry and R. C. Ricks

*Radiation Emergency Assistance Center/Training Site, Oak Ridge Associated Universities, Oak Ridge, Tennessee, USA*

Until the recent radiation accident in Chernobyl, the medical basis for the care of victims of radiation accidents was derived from relatively few events and patients. In over 40 years, since 1945, only 284 accidents have occurred, resulting in serious radiation exposures to 619 persons with fatal outcomes in only 31 cases. Even so, these medical experiences, which have been carefully annotated and studied worldwide at such radiopathology centres as the US Department of Energy Radiation Emergency Assistance Center and Training Site (REAC/TS) in Oak Ridge, comprise the bulk of human radiation biology that served, in part, in shaping the medical care that the more than 200 severely irradiated Chernobyl accident victims received That experience, still known to us only in fragmentary fashion, significantly increased the information in the REAC/TS Radiation Accident Registry and revealed the great clinical importance of non-radiation injuries in determining the nature of medical assistance and final outcome of otherwise sublethal radiation exposures. Previously, the kind of accident radiation injury of greatest incidence in civilian life involved local rather than total-body exposures. These injuries caused great debility but rarely were fatal. Now we must be aware that radiation when combined with traumatic injuries poses greatly magnified problems for medical management yet to be resolved.

*This program is conducted for the US Government under Contract No DE-AC05-760R00033.

### MEDICAL BASIS FOR THE ESTABLISHMENT OF INTERVENTION LEVELS

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The establishment of intervention levels for the various countermeasures, whatever the reference system chosen, requires the best possible knowledge of the effects likely to appear in the population exposed to radiation following an accident. Non-stochastic effects can appear in well defined organs or tissues: principally, bone marrow, lung, thyroid and skin, and, where pregnant women suffer exposure, the fetus. The shape of the dose–effect curves for most of these organs is, in general, sufficiently well known, as are the thresholds at which the effects appear Nevertheless, the degree of uncertainty in doses which are of main interest, *i.e.* the threshold doses, and the doses responsible for 50% and 100% of the effects, is, in some cases, of the same order of magnitude as the $D_0$–$D_{100}$ interval. These differences make it difficult to give a quantitative prognosis for the likelihood of survival in a population which may be exposed within the dose range proposed for $LD_{50/60}$. However, it is likely that the data needed for correct decisions need neither to be refined nor to include all the known data about the effects of radiation on each organ or system. The main point is to appreciate the dose levels below which, in a normal population, the probability of non-stochastic effects appearing is practically zero As the first basic principle for protecting the public in case of a nuclear accident is to avoid serious non-stochastic effects, by countermeasures to limit individual dose to levels below the thresholds for these effects, the competent authorities should base their choice of intervention levels on these thresholds The second basic principle, *i.e.* limiting the risk from stochastic effects by introducing countermeasures which achieve net benefit to the individuals involved, should be considered as a secondary step in the establishment of intervention levels.

## Session II

**Chairman: Professor R. J. Berry**

UK nuclear reactor design and operation, by B Edmondson No abstract received
UK nuclear power station emergency plans, by J K. Wright. No abstract received
UK reactor accident preparedness: medical considerations, by R. A. F. Cox No abstract received
Reactor accident preparedness: medical considerations, by A Barrett No abstract received
Reactor accidents in perspective, by R. H. Clarke

### REACTOR ACCIDENTS IN PERSPECTIVE

Roger H. Clarke

*National Radiological Protection Board, Chilton, Didcot*

There have been three reactor accidents which have led to significant releases of radionuclides to the environment and subsequent exposure of members of the public. These are the Windscale accident in the UK in 1957, that at Three Mile Island (TMI) in the USA in 1979, and the Soviet Chernobyl accident in 1986 This paper outlines the cause of each accident and why the composition of released radionuclides differed: iodine 131 and polonium 210 were important at Windscale, xenon 133 at TMI, and principally iodine 131 and caesium 134 and 137 at Chernobyl

Although the release of xenon 133 from TMI was greater than that of iodine 131 from Windscale, the effective dose equivalent to the most exposed individual members of the public were about 10 times lower For Chernobyl, the total activity released was about 10 times greater than from TMI, and the off-site doses were several hundred times higher. These differences are explained by the differing pathways of exposure of the population to the different radionuclides

The total health impact of the three accidents will be put into perspective by comparing doses and the associated presumed risks with other sources of dose and risk to which the population are exposed in every-day life. While there is a presumption of linearity, without a threshold, between dose and risk, there will always be a need to argue for a level of acceptable risk to members of the public. This led to conflicts of statements that, on the one hand, the individual risk is negligible, say one in a million, and there need be no concern, and, on the other hand, that because 50 million people were exposed there may be as many as 50 deaths. Both statements are true but the public, or at least the media, found them irreconcilable

## The Diagnosis and Management of Early Breast Cancer

**Chairman: Dr R. Buchanan**

Paper by I. Taylor. No abstract received
Paper by P. B Guyer. No abstract received

## Central Nervous System Trauma

**Chairman: Dr E. H. Burrows**

Head trauma. computed tomography and prognosis, by I. R Colquhoun
Radiology of the spine and spinal cord injury, by P L. Cook

### HEAD TRAUMA: COMPUTED TOMOGRAPHY AND PROGNOSIS

I. R. Colquhoun

*Department of Neuroradiology, Southampton General Hospital*

A review of the computed tomographic findings associated with severe head trauma is presented. Attention is drawn to certain signs, which though not visually dramatic, have significant implications for the management of acutely ill patients and for their eventual prognosis

### RADIOLOGY OF SPINE AND SPINAL CORD INJURY

P. L. Cook

*Department of Radiology, Southampton General Hospital*

The patterns of injury to the cervical and thoraco-lumbar spine are presented. Concepts of spinal stability are discussed together with the roles of conventional radiography, computed tomography and myelography in assessing stability and the extent to which the spinal canal is compromised.

# Techniques of Flow Measurement

**Chairman: Dr M. A. Smith**

Flow measurements using ultrasound, by W. N. McDicken No abstract received
Flow measurement using nuclear magnetic resonance, by M. A. Smith

## FLOW MEASUREMENTS USING NUCLEAR MAGNETIC RESONANCE

M. A. Smith

*Department of Radiological Sciences, Guy's Hospital, London*

There are several techniques that can be used to measure flow velocity; of these the two methods of Doppler ultrasound and nuclear magnetic resonance (NMR) imaging are relatively recent developments In addition to imaging flow, both techniques can be used to obtain quantitative flow measurements The physical principles of the two methods are described with examples of their application

Simple and duplex Doppler systems are described, as are Doppler flow mapping and Doppler sonograms. The latter show velocity–time curves of blood cells. The intensity and power output of Doppler units are discussed with relevant safety considerations. Applications in the fields of obstetrics, paediatrics and cardiology, amongst others, are presented.

Flow can influence the intensity of the signal in an NMR image by paradoxical enhancement. However, if an appropriate pulse sequence is used it is possible to encode velocity information in the phase of the NMR signal. Methods to obtain phase maps, which contain quantitative information concerning the amplitude and direction of movement, are described. Images of high and low blood flow and cardiac wall motion are presented.

# Paediatric Radiology

**Chairman: Dr R. K. Levick**

A retrospective study comparing the quality of intravenous pyelograms in infants using iohexol, sodium diatrizoate and metrizamide as contrast agents, by J. Rawlinson and I. Hyde
The changing pattern of bronchopulmonary dysplasia· time for a new look? By R E English and I. Hyde
Changes in the management of intussusception, by R. A. Paes, I. Hyde and D M Griffiths
Radiation limitation in the special-care baby unit, by B. Danby

## A RETROSPECTIVE STUDY COMPARING THE QUALITY OF INTRAVENOUS PYELOGRAMS IN INFANTS USING IOHEXOL, SODIUM DIATRIZOATE AND METRIZAMIDE AS CONTRAST AGENTS

J. Rawlinson and I. Hyde

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The intravenous pyelograms (IVPs) from 283 infants, ranging in age from 1 day to 1 year, were reviewed and assessed for quality. Iohexol (Omnipaque 300, Nycomed) was used as contrast agent in 94 patients, sodium diatrizoate (Hypaque 270, Winthrop) in 98 patients and metrizamide (Amipaque 280, Nycomed) in 91 patients Seventeen of the IVPs were excluded on the basis of poor renal function, leaving a total of 86 in the iohexol group, 95 in the diatrizoate group and 85 in the metrizamide group. In the Diatrizoate and metrizamide groups the patients were well matched for age (mean age 8 4 weeks and 9.7 weeks, respectively) compared with a mean age of 14.6 weeks in the iohexol group. No serious adverse side-effects were encountered The quality of the IVPs was assessed using similar criteria to that described by Kelsey Fry et al (1967) with a maximum total score of 52. For each IVP the film most clearly demonstrating the anatomical part in question was selected for assessment. The results are presented.

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Kelsey Fry, I, Cattell, W R., Spencer, A G & Purkiss, P., 1967 II The relation between Hypaque excretion and the intravenous urogram. *British Journal of Radiology, 40,* 572–580

## THE CHANGING PATTERN OF BRONCHOPULMONARY DYSPLASIA: TIME FOR A NEW LOOK?

R. E. English and I. Hyde

*Wessex Department of Paediatric Radiology, Southampton General Hospital*

Hyaline membrane disease in premature infants is sometimes complicated by a chronic pulmonary disease which requires prolonged administration of supplemental oxygen and/or mechanical ventilation The evolution of the radiographic appearances of this chronic lung disease (bronchopulmonary dysplasia) is described as a characteristic pattern of emphysematous cysts interspersed with strands of density However, the pattern now being seen in a majority of chronically oxygen-dependent or ventilator-dependent premature infants is different. A group of 34 infants with chronic lung disease is described, 19 of whom did not conform to the classic pattern.

## CHANGES IN THE MANAGEMENT OF INTUSSUSCEPTION

R. A. Paes, I. Hyde and *D. M. Griffiths

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Hydrostatic reduction is now the first line of treatment of intussusception. Many aspects of management have changed and some of the contraindications to barium enema, which have, in the past, been considered important, are no longer valid. Radiological proof of reduction is no longer the sole criterion for success and more emphasis is now placed on clinical improvement. If there is doubt concerning success there is an increasing readiness to repeat the procedure, after an interval, if the clinical condition permits. It is now more important than ever that these decisions are made in close collaboration with the paediatric surgical team

### RADIATION LIMITATION IN THE SPECIAL-CARE BABY UNIT

Brenda Danby

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It has been estimated that two cases of malignant disease may annually be caused by diagnostic radiography of the newborn child Premature or low-birth-weight babies with respiratory distress syndrome are likely to have a considerable number of radiographs during the first few weeks of life Radiation risk is minimised by making sure that only essential radiographs are taken Education, accurate radiography, precise coning, including lead placed on top of the incubator to reduce scatter, rare-earth screens, fast films, and cassettes made of low-attenuation material all play their part. In addition, regular maintenance and testing of equipment will ensure that optimum images are always obtained. Extensive tests have been carried out, in Southampton, to assess many of the film–screen combinations currently available, particular emphasis being placed on speed, latitude, granularity, contrast and resolution We have recently looked at the attenuation of various plastic and carbon-fibre cassettes available and the exposure factors required to maintain film quality The results are discussed.

## Value for Money—Getting Equipment for the National Health Service

**Chairman: Mr J. A. Garrett**

An introduction to the centres of responsibility, by M D Ensor
Clinical needs and priorities, by G. Hartley
Specification. what, how, why, by A J Sargood
Patterns of procurement in the NHS, by M. R. Eddy
The management and allocation of equipment, by C. Darby

### AN INTRODUCTION TO THE CENTRES OF RESPONSIBILITY

M. D. Ensor

*Regional Supplies, South East Thames Regional Health Authority*

Centres of Responsibility were created by the Supply Council with the aim of developing and maintaining product-related policies in the NHS. This work had previously been undertaken by the DHSS Since the demise of the Supply Council the overview and control for the development of the Centres of Responsibility have come under the Director of Procurement. The concept of the Centres of Responsibility is not just national contracting but embraces the wider aspects of policy, objectives and forward planning, and serves as a vital communication link between industry and the NHS.

The South East Thames Regional Health Authority was allocated radiology equipment, maintenance and silver recovery and initially established a Commodity Advisory Group as a policy-making body. The Commodity Advisory Group membership includes representatives from radiology, radiography, works, finance, scientific and technical department, regional scientific officers and supplies The Centre of Responsibility operates according to a defined work programme agreed by the Commodity Advisory Group. The individual work plans are not cast in concrete and it is the Centre of Responsibility's published aim to be responsive to the trade and to the NHS. Meetings are held with both whenever appropriate.

Working parties have been created to examine in depth the operation of certain facets of diagnostic radiology and currently are examining the following areas operational requirements and performance specifications; roles and responsibilities of all concerned with the procurement and maintenance of equipment for diagnostic radiology; maintenance of X-ray and associated equipment, and methods of supply and use of X-ray tubes in the NHS.

### CLINICAL NEEDS AND PRIORITIES

Geoffrey Hartley

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The definition of clinical need in general terms is discussed and, by using the statistics of an X-ray department, the point of view of the clinical radiologist is presented, *e g.* how many computed tomography (CT) scanners are needed? Detail of management techniques in a busy teaching hospital department is given showing how the annual equipment schedule in priority order is achieved Some of the arguments supporting the final draft are given, concentrating on specific examples such as CT, ultrasound, mammography, and angiography The progress of the request is then traced through the current bureaucracy to the final decision to purchase. The recent pressure to produce greater precision by accurate specifications is discussed with an attempt to assess the success of specifications and tendering in achieving better value for money A personal view on a method for equipment purchase for the NHS is presented

### SPECIFICATION: WHAT, HOW, WHY

A. J. Sargood

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In the past, equipment procurement often meant the user specifying the make and model of the equipment required. With the emphasis now on achieving value for money, there is a move towards either competitive tendering or informal negotiations with competing suppliers. In either case, the suppliers are required to tender/quote against an equipment specification. The specification then becomes an important document which must reflect the clinical requirement and contain sufficient technical detail to fulfil that requirement

The starting point is, thus, the clinical need, which is normally couched in terms of a technical requirement that may well exceed the real need. The manner in which a realistic technical requirement is achieved is a contentious issue but, nonetheless, important. The requirement is then converted to a full specification by adding the necessary technical detail and removing any bias towards a specific manufacturer. Compliance with national standards, maintenance and training, all need to be included The second aspect of procurement is the acceptance of and payment for the equipment Here too the specification is important, as it is against this document that acceptance checks and measurements are made It is therefore essential that the specification contains sufficient detail to allow testing to demonstrate the required equipment performance.

The importance of the specification is apparent but the question of who writes it then arises Since there is unlikely to be a single person knowledgeable about all types of imaging equipment it is desirable that the specification be derived in conjunction with the users

### PATTERNS OF PROCUREMENT IN THE NHS

M. R. Eddy

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The Roles & Responsibilities Working Party was commissioned to examine how regions obtain radiology equipment and how individual functions relate to the procurement process. Although the NHS is nominally a single body, with the inception of direct tendering differing approaches to the same subject have developed, reflecting the fact that radiology procurement crosses many boundaries and hierarchical structures.

What should be the best possible level or system to obtain equipment taking into account not only price but other factors, such as pre-installation work and revenue consequences including maintenance? The Centre of Responsibility is in a unique position to overview the differing policies and procedures within the NHS and make recommendations A region may well consider that it is approaching the process in a correct manner, but consideration should be given to other, more cost-effective systems. There are vast differences in the level of involvement of the various categories of personnel across the country and these differences are illustrated. The appropriate input from each discipline at each stage of the procurement process has been noted in respect of the regions visited and this is compared with a model form of personnel designated to operational functions. The aim is to produce guidelines that would enable the most effective system for any given set of options which are capable of being applied and accepted by the NHS to be developed Only in this way will the NHS realise true value for fully costed options.

### THE MANAGEMENT AND ALLOCATION OF EQUIPMENT

C. Darby

*South East Thames Regional Health Authority*

Previous contributions in this session have dealt with clinical need, specification, and procurement patterns for medical and scientific equipment

Each region adopts an equipment allocation policy which is largely dictated by its local arrangements for the assessment of clinical need, and its particular regional purchasing policy. In recent years it has proved impossible for many regions to replace ageing equipment at reasonable intervals, partly because of the large amount requiring replacement, but also because of limited regional capital available to fund the equipment-replacement programme.

If we assume that the average regional medical equipment budget will remain substantially the same in real terms for the foreseeable future, then, unless a new philosophy is adopted for the allocation and management of equipment, we shall be locked into a cycle of ever increasing intervals between capital equipment replacement. This paper explores some of the changes that may be necessary to the allocation and management of equipment if we are to shorten the replacement interval and, at the same time, live within the current capital cash constraints.

## Radiotherapy

**Chairman: Dr F. Neal**

The treatment of pleomorphic adenomas of the parotid using a mixed-schedule (photons/electrons) technique, by P J. D K. Dawes and G. Lambert

Pattern of lymphomas in Kasturba Hospital, Manipal, by V. Balasundaram, M S. Vidyasagar and J. G. R. Solomon

The use of magnetic resonance imaging in radiotherapy treatment planning, by S C Bolton

Focal and generalised pneumonitis following bone marrow transplantation for chronic myeloid leukaemia, by A M K. Thomas, C Arthur, J. F. Apperley, A W. G. Goolden, J M Goldman and J P Lavender

Haemoglobin, blood pressure, radiation myelitis and survival in carcinoma of the bronchus, by S Dische and M F Warburton

A randomised trial of tamoxifen versus radiotherapy for Stage III breast cancer. early results, by D Gilson, M R Williams, L March, R W Blamey and D A L Morgan

The detection of extraluminal local recurrence in rectal cancer, by J. Beynon, N. J. McC Mortensen, D M A Foy, J L channer and J Virjee

The ultrasonic consequences of radiation therapy to the rectum, by J Beynon, N J McC. Mortensen, D M. A. Foy, J L Channer and J Virjee

Osteosarcoma and other neoplasms of bone a possible contribution of phosphorus-31 magnetic resonance spectroscopy to therapeutic monitoring, by B D. Ross, I. J Cox, J Pennock, H A Case, I. R Young, D R. Bailes, D J Bryant, A Makepeace, J Pringle and A N Sweetnam

The use of magnetic resonance imaging in the assessment of the response of cervical tumour to therapy, by A. W L Leung, J. W Lecky, E Grosch, M. Saunders and S. Dische

The use of lymphoscintigraphy for estimating the dose to the axillary lymph nodes in breast cancer radiotherapy, by B Planskoy, A M. Bedford, L. T. Loverock and P. J. Ell

High dose rate or low dose rate in gynaecological contact therapy? By R. Schulz-Wendtland, M. Bauer, D. v Fournier and H A. Ladner

A remote interstitial afterloading system, by J. W Scrimger, A T Porter and J S Pocha

### THE TREATMENT OF PLEOMORPHIC ADENOMAS OF THE PAROTID USING A MIXED-SCHEDULE (PHOTONS/ELECTRONS) TECHNIQUE

P J D. K. Dawes and *G. Lambert

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Pleomorphic adenomas of the parotid (mixed salivary tumours of the parotid) are benign tumours which have a tendency to recur locally if the tumour is not removed intact with a large amount of normal gland completely enclosing the tumour. Radiotherapy is indicated for these tumours in two circumstances if the tumour has been excised without removing the surrounding gland or if the tumour pseudocapsule is ruptured during treatment.

Two series have been reported from Newcastle upon Tyne and only eight of 256 had recurred. The most usual treatment method was a direct field from a $^{137}$Cs teletherapy unit. This machine was removed some years ago because it had a low dose rate. A mixed-schedule technique employing $^{60}$Co photons and 14 MeV electrons has been used. The rationale of this technique is discussed and compared with alternative techniques. Twenty-three patients have been treated without undue morbidity or recurrence.

### PATTERN OF LYMPHOMAS IN KASTURBA HOSPITAL, MANIPAL

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A retrospective analysis of 209 patients with lymphomas was conducted with a view to studying the pattern of disease, investigations and treatment results. Almost all patients were managed on the lines recommended by the British National Lymphomas Investigation Protocol, with minor modifications to suit our set-up. Out of 209 patients seen between 1979 and 1984, around 62% had non-Hodgkin's lymphomas. One hundred and fifty-four patients presented with Stage III and Stage IV disease, whereas only 55 patients were seen with early disease. All investigations necessary to establish the diagnosis, staging and assessment of prognosis were undertaken before embarking upon definite treatment. Staging laparotomy was not routinely done. Bipedal lymphangiograms have not been done since an ultrasound scanner and a whole-body scanner were installed. The majority of the patients are observed to have low haemoglobin with elevated erythrocyte sedimentation rates. Serum copper level was determined in most of the cases and was found to be elevated in 42%. It is a helpful prognostic indicator, as patients with initially high serum copper levels returned to normal whenever they responded to treatment. Pattern of clinical involvement and other investigation reports, as well as survival data, are presented.

### THE USE OF MAGNETIC RESONANCE IMAGING IN RADIOTHERAPY TREATMENT PLANNING

S C. Bolton

*Department of Medical Physics, Leicester Royal Infirmary*

It is essential, when planning radiotherapy treatment, to ensure that the tumour volume is well defined in all three dimensions. Magnetic resonance (MR) imaging can image tumours exceptionally clearly, but in order to be useful for treatment planning, the tumour volume must be accurately related to the surface of the patient. This is especially critical in planning treatment to the head and neck. Markers have been designed which can be attached to the beam-direction shell and be clearly seen on a simulator radiograph and on computed tomography (CT) and MR scans. A surface coil has been constructed to improve the resolution of MR scans performed on patients wearing a beam-direction shell The shell ensures that the patient is in the same position for the CT and MR scans and so direct comparisons can be made between the imaging techniques Their relevance to radiotherapy treatment planning is assessed.

## FOCAL AND GENERALISED PNEUMONITIS FOLLOWING BONE MARROW TRANSPLANTATION FOR CHRONIC MYELOID LEUKAEMIA

A. M. K. Thomas, *C. Arthur, *J. F. Apperley, †A. W. G. Goolden, *J. M. Goldman and J. P. Lavender

*Departments of Radiology, *Haematology and †Radiotherapy, Hammersmith Hospital and Royal Postgraduate Medical School, London*

The chest radiographs of 64 patients treated for chronic myeloid leukaemia (CML) by allogenic bone marrow transplantation were reviewed. Forty-nine patients were in the chronic phase and 12 were in a more advanced phase of CML. They were treated by high-dose chemoradiotherapy consisting of cyclophosphamide (60 mg/kg × 2) and total-body irradiation (10 Gy or 12 Gy in five or six fractions) delivered by a linear accelerator at a source distance of 500 cm and a dose rate of 15 cGy/min without lung shielding. All patients in this series retained their spleens and were treated with radiotherapy to the splenic area (10 Gy in two fractions) in addition to the total-body irradiation. The majority received T-cell depleted donor marrow, and all received cyclosporin post-transplant for prevention of graft versus host disease Thirty-one (51%) patients developed radiographic changes. Twenty-one (33%) developed pneumonic changes within 3–308 days (mean 112 days) which were usually generalised. Twelve (57%) of these 21 patients died, the organism being most commonly cytomegalovirus Localised consolidation commonly associated with pleural shadowing was observed in the latero-basal or postero-basal segment of the left lower lobe in a further 13 patients (20%) with radiographic changes developing from 48–179 days (mean 107 days). The patients were usually asymptomatic or had only minor respiratory symptoms The appearances were thought in some to be infective in nature but no organism was discovered and the changes slowly regressed spontaneously over a period of several months Four of these patients with initial left basal consolidation later developed more generalised consolidation associated with a clinically obvious infection and one of these patients died In this series there is a high incidence (33%) of chest radiographic changes due to infection. However, other patients with focal left basal consolidation have a benign course; these changes are probably due to the combined effects of the total-body irradiation and the local splenic irradiation that involves adjacent lung.

## HAEMOGLOBIN, BLOOD PRESSURE, RADIATION MYELITIS AND SURVIVAL IN CARCINOMA OF THE BRONCHUS

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A data bank has been established which includes all 710 patients who survived more than 6 months after radiotherapy for carcinoma of the bronchus given during the period January 1966 to December 1984. Previous analyses have shown an incidence of radiation myelitis in patients treated with six fractions, using opposing portals, without cord shielding. This complication occurred above a threshold cord dose of 33.5 Gy. Considering the cases at risk the incidence has been shown to be influenced by the haemoglobin concentration at the time of treatment. In these same patients survival was significantly greater in those given a higher radiation dose and was also greater in those with a higher haemoglobin concentration. We have now shown in these patients that the systolic blood pressure or the pulse pressure, but not the diastolic blood pressure, can also be directly correlated with survival, it is not, however, related to the incidence of radiation myelitis. Following the institution of cord shielding for part of the treatment, after 1978, those similarly treated were not, in terms of survival, affected by any of these prognostic factors Evidence has accumulated to suggest that this is related to the need for a threshold radiation dose to be achieved, for only when this is achieved can factors which may influence tumour control be expected to show effects. Cord shielding gives an underdosing in part of the tumour volume and brings the effective tumour dose below this threshold. These findings have important implications for the attempted cure of tumours by radiotherapy.

## A RANDOMISED TRIAL OF TAMOXIFEN VERSUS RADIOTHERAPY FOR STAGE III BREAST CANCER: EARLY RESULTS

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Eighty-seven post-menopausal women have been randomised to either tamoxifen ($n = 43$) or radiotherapy ($n = 44$), as first-line treatment for locally advanced breast cancer. Treatment was "crossed-over" on disease progression or after 6 months if there was no response. Response was assessed using British Breast Group criteria Time to metastases, survival and duration of response were examined by life-table analysis. The median follow-up was 24 (range 9–46) months

After 6 months there was response in 19 cases treated with tamoxifen, no change in 13 and disease progression in 11. After 6 months of radiotherapy there was response in 30 cases, no change in six and disease progression in eight. Response does not relate to oestrogen receptor status. Disease progressed despite "cross-over" in six patients in each group. At analysis, 13 patients from the tamoxifen group had not required local radiotherapy. There was no significant difference on log-rank analysis in time to metastases (35 events), survival (22 events) or duration of response to initial treatment. Despite a higher initial response rate in the radiotherapy group, there was no significant difference in rate of disease progression after 6 months, in overall survival or in time to development of metastases. These early results suggest that the use of tamoxifen as primary treatment is safe, and spares some patients radiotherapy, but further recruitment and longer follow-up will be needed to confirm this

## THE DETECTION OF EXTRALUMINAL LOCAL RECURRENCE IN RECTAL CANCER

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Locally recurrent rectal cancer is invariably detected late, when no further surgical treatment can be offered. The mechanism of the recurrent disease is thought to be twofold: extraluminal and suture-line recurrence. Routine sigmoidoscopy should be able to detect suture-line recurrence but not extraluminal disease until it is well advanced. We have assessed the effectiveness of rectal endosonography (ES) in the routine follow-up of 72 patients who had previously undergone surgical treatment for rectal cancer. In total, 11 recurrent rectal cancers have been examined at various stages of gestation. In this group three tumours were detected solely by ES as extrarectal ultrasonic abnormalities. In all cases the endosonographic evaluation has provided information for the more detailed planning of management. The use of ES in this way will hopefully allow the early diagnosis of recurrent disease and, thus, its effective treatment.

## THE ULTRASONIC CONSEQUENCES OF RADIATION THERAPY TO THE RECTUM

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Endosonography has been shown to be an effective method for the pre-operative staging of rectal cancer, allowing the more precise planning of surgical options and the inclusion, in appropriate cases, of radiotherapy as an adjuvant treatment. In 93 cases studied to date, some have been treated with adjuvant pre-operative radiotherapy. We have noted that this can alter the ultrasonic appearances of the normal rectum. In these patients the normal five-layered ultrasonic image of the rectum may be replaced by a three-layer image due to mucosal/submucosal fibrosis. Additionally, it may be difficult to differentiate reactive tissue from the primary tumour and to identify pararectal lymph nodes. Similarly, the use of post-operative radiotherapy can make the detection of early extraluminal local recurrence difficult because of the presence of reactive tissue. In this situation transperineal or trans-abdominal biopsy is the only certain method of excluding the presence of secondary neoplasm.

## OSTEOSARCOMA AND OTHER NEOPLASMS OF BONE. A POSSIBLE CONTRIBUTION OF PHOSPHORUS-31 MAGNETIC RESONANCE SPECTROSCOPY TO THERAPEUTIC MONITORING

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The feasibility of obtaining $^{31}P$ magnetic resonance spectra from human extremity bone tumours was demonstrated in four patients by Neideker et al (1985). We present our experience of more than 14 such patients in whom magnetic resonance imaging (MRI) and $^{31}P$ magnetic resonance spectroscopy (MRS) examinations have formed part of the routine pre-treatment investigation. Furthermore, in seven patients we have carried out repeated $^{31}P$ examinations to record the early and late alteration in tumour metabolism consequent to chemotherapy. Patients were referred from the Oncology Unit, Middlesex Hospital, aged 8–57 years and MRI was carried out at Hammersmith Hospital (0.15 T) and MRS (1.6 T) on a Picker research instrument. The $^{31}P$ spectra, obtained from the sensitive volume of a surface coil, illustrated reproducible abnormalities in all but one patient (the exception was a subject in whom the spectrum was too poorly resolved). The principal abnormalities, increased adenosine triphosphate, phosphodiester and phosphomonoester peaks, were accompanied by an increase in inorganic phosphate. However, intratumour pH was normal. Spatially localised spectroscopy yielded additional information, in particular by defining the phosphocreatine level in tumours. No correlation of $^{31}P$ MRS with histology or tumour stage has been established. In response to treatment (and time), tumour spectra changed in all seven subjects studied. In particular, the phosphomonoester peak receded, in one patient, a normal muscle spectrum resulted. The progress of tumour regression was more accurately mapped by using spatially localised spectra. In general we predict useful qualitative and quantitative information will be obtained in studies using MRI and MRS in combination during the treatment of limb tumours.

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## THE USE OF MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF THE RESPONSE OF CERVICAL CARCINOMA TO THERAPY

A. W. L. Leung, J. W. Lecky, E. Grosch, M. Saunders and S. Dische

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It has been shown that magnetic resonance imaging (MRI) can sharply delineate the carcinoma of the cervix within the cervical stroma, as well as showing its extension into the body of the uterus and vagina. However, there are certain pitfalls in demonstrating parametrial, rectal and bladder, and pelvic lymph-node involvement. The application of MRI in the assessment of the response of cervical tumour to radiotherapy and chemotherapy has been very useful. High-resolution images of the cervical tumour can be obtained by using a small-field diameter, a 256 × 512 matrix, contiguous 5 mm multislice imaging in the sagittal and transverse planes and spin-echo 1200/60 sequences. This, in turn, allows measurements of tumour volume.

A long-term study of tumour response to therapy using MRI is being carried out. To date, 82 patients with cervical carcinoma have been studied. A total of 168 examinations have been carried out and 30 patients had two or more examinations. The change in the tumour volume can be plotted against time. The rate of tumour regression, and hence the volume-halving time, can be calculated. Initial good response to irradiation or chemotherapy has been observed and regrowth of tumour was observed in some patients 60–80 days after the start of therapy. The optimal interval for follow-up examination for early detection of tumour regrowth is discussed.

## THE USE OF LYMPHOSCINTIGRAPHY FOR ESTIMATING THE DOSE TO AXILLARY LYMPH NODES IN BREAST CANCER RADIOTHERAPY

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There is considerable interest in relating efficacy and complications of axillary radiotherapy to the absorbed dose

Published data (Brinkley et al, 1984) show that local recurrence in the axilla is reduced in patients who have received radiation treatment. However, for these patients, there appears to be no obvious reduction in local recurrence with increased stated dose, over a wide range of doses One possible explanation for this could be that the "stated" dose to the axillary midline does not always represent the best estimate of the "actual" dose received by the axillary lymph nodes We have used a standard method of lymphoscintigraphy to obtain orthogonal images of the main collecting axillary nodes and, hence, three-dimensional reconstruction of the position of these nodes in relation to the radiotherapy treatment fields. This enabled us to compare the "actual" and "stated" doses to the nodes

We have so far obtained satisfactory images for 26 out of 33 patients. The preliminary results show that in nine of these 26 patients the actual doses were considerably lower than the stated midline doses. In particular, in seven of eight patients whose treatment protocol included a posterior axillary boost field, the latter field was shown only partially to cover the nodes. Details of the method and of results to date are presented

We wish to thank Professor R. J Berry, Dr C. Coulter, Dr A. M. Jelliffe and Dr M. F. Spittle of the Meyerstein Institute of Radiotherapy for referring their patients

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## HIGH DOSE RATE OR LOW DOSE RATE IN GYNAECOLOGICAL CONTACT THERAPY?

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In contact therapy the advantages of high dose rate over low dose rate brachytherapy are obvious Outpatient treatment becomes possible, the position of the sources is reproducible and can be supervised during the treatment, and the patients have to be immobilised for only a short time, giving less psychological stress and a decreased risk of thrombosis and embolism We therefore carried out experiments with nine Gottingen minipigs to compare the biological reaction of healthy tissue after contact therapy using a low dose rate (three fraction of $^{226}$Ra) with that using a high dose rate ($^{192}$Ir, different reduction of dose, six fractions). The treatment time was the same Moreover, we wanted to gain information about the importance of protraction and fractionation The results demonstrate that it is possible to indicate an equivalent dose for the entire target volume only for defined source distances. To get equivalent biological effectiveness near the sources, more healthy tissue will be destroyed using a high dose rate. To protect healthy tissue in the periphery in a comparable way, it is possible to use a low dose rate, with greater efficiency near the sources. Thus, close to the sources, the dose is decisive; further from the sources, the dose rate becomes the more important.

## A REMOTE INTERSTITIAL AFTERLOADING SYSTEM

J. W Scrimger, A. T. Porter and J. S. Pocha

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We have recently instituted the use of a remote afterloading system, after a period of joint development between ourselves and the supplier (Nucletron Corporation) This system, with the trade name "Microselectron", is designed to transport interstitial· brachytherapy sources to previously implanted needles The sources can be radioactive $^{192}$Ir wire, $^{192}$Ir seeds in plastic tubing, or $^{137}$Cs beads in a specially designed transport tube Our experience has been with $^{192}$Ir seeds in plastic tubing and it is this work which we present.

The Microselectron system has three principal components, viz the source preparation station, the source storage container, and the Microselectron Radioactive seeds with a predetermined activity arrive at the hospital in a lead transport container. They are prepared for use in the Microselectron at the source preparation station, and are then transferred to the storage container without exposure to the operator The mobile storage container is then moved to the ward where the Microselectron is used, and some of the sources are moved from the storage container to the Microselectron. The latter has a capacity for a maximum of 15 ribbons, but sources can be readily moved back and forth between the Microselectron and the storage container.

In this paper we present some of the clinical advantages which can be realised by the use of such a system These include variable loading of the insertion, both with respect to time and activity Dose reduction to all staff, particularly the radiotherapist and the nursing staff, is of paramount importance, and is consistent with the "as low as reasonably achievable" principle. We also describe some of the technical developments which have taken place in our hospital, in conjunction with the manufacturer, which have enabled us to overcome most of the initial difficulties with each sub-component in the system and, finally, we attempt to evaluate the implications of remote afterloading for future brachytherapy.

# Clinical: Musculo-Skeletal and Breast

**Chairman: Dr J. T. Patton**

The use of short $T_1$ inversion-recovery sequences in the evaluation of spinal pathology, by B. S. Worthington, M Gibson, B. J Preston, R. C Mulholland and P. Szypryt

The role of magnetic resonance imaging in the management of lumbar spondylolysis, by P Twining, B. S. Worthington, P. Szypryt and W Mulholland

Computed tomographic myelography in the investigation of childhood scoliosis and spinal dysraphism, by C. I Rothwell and W St. C Forbes

Parasymphyseal insufficiency fractures, by A. M Davies and N Evans

Chimpanzee hip? By C. W Hutton and I Watt

Synovial chondromatosis, by M D. Crone, H. Maurice and I Watt

Tumoral calcinosis response to phosphate deprivation, by J. E Adams and M. Davies

The use of sonomammography in assessment of volume change in primary carcinoma of breast in response to adjuvant therapy, by T F El Sayed, R Ashford, K Blenkinsopp, S. Cox, A Horsburgh and H. Nath

Training in mammographic interpretation, by A G Gale, S. E Downey, E. J Roebuck and B. S Worthington

Doppler ultrasonography of an experimental soft-tissue tumour the effects of a vasoconstrictor, by P M. Taylor, S. Rimmer, B. Moreman and I Isherwood

## THE USE OF SHORT $T_1$ INVERSION-RECOVERY SEQUENCES IN THE EVALUATION OF SPINAL PATHOLOGY

B. S. Worthington, *M. Gibson, B. J. Preston, *R. C. Mulholland and *P Szypryt

*Departments of Academic Radiology and *Orthopaedic Surgery, University of Nottingham*

The use of a short $T_1$ inversion-recovery sequence with a spin-echo data collect and modulus reconstruction has a number of advantages in studying spinal pathology. The $T_1$ and $T_2$ contrasts are additive after the final 90° pulse and this produces a high total contrast in disorders where both the $T_1$ and the $T_2$ relaxation times are lengthened. By choosing a $T_1$ value of 100 ms when imaging at 0.15 T with a resistive system, the signal from fat is suppressed whereas the signal from cerebrospinal fluid (CSF) is extremely high, giving an excellent delineation of thecal boundaries. This sequence has been used along with conventional $T_1$- and $T_2$-weighted sequences in a number of protocols evaluating spinal pathology and the following additional information has accrued

(1) In a group of patients studied after a single-level chemonucleolysis, transient high-signal zones were noted adjacent to the vertebral end-plates These changes probably reflect a mild chemical discitis. No similar changes were noted in a control group having discography only (2) Frank disc space infection and paravertebral abscess, although clearly recognisable on $T_2$-weighted sequences, were highlighted with the sequence. (3) In rheumatoid arthritis involving the atlanto-axial articulation the sequence is superior to all others in highlighting the pannus (4) The soft-tissue extensions of tumours involving the vertebral column were accurately defined by the use of this sequence, although the relationship of any intraspinal component to the cord was better shown with sequences which give a fuller display of the relevant anatomy, *e g* a short TR, short TE spin-echo sequence. (5) The signal from CSF is extremely high with this sequence and this allowed stenotic lesions of the theca to be clearly defined at all levels

## THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE MANAGEMENT OF LUMBAR SPONDYLOLYSIS

P. Twining, B. S. Worthington, *P. Szypryt and *W. Mulholland

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A consecutive series of 40 symptomatic patients with a known lumbar spondylolysis affecting either the fourth or fifth vertebra was studied prospectively using a 0.15 T resistive magnet system. The integrity of the intervertebral disc at the level of the spondylolysis was assessed using a sagittal $T_2$-weighted spin-echo sequence and the same sequence was used to assess an asymptomatic control group of age- and sex-matched volunteers. In 15 of the 17 patients within the 11 to 25 year age group, magnetic resonance scanning revealed a normal disc at the level of the spondylolysis Disc degeneration was seen in 12 out of 15 of the 25 to 35 year age group; however, the majority of changes were moderate. All patients over 35 years old, however, demonstrated severe disc degeneration at the level of the spondylolysis Comparison with the control group revealed a markedly higher than expected incidence of disc degeneration at the level of spondylolysis and this suggests that the presence of a spondylolysis accelerated disc failure The implications for treatment are that under 25 years of age a repair of the spondylolytic defect alone is adequate; for the older age group, this should be accompanied by a stabilising procedure such as a spinal fusion at the level of the lysis

## COMPUTED TOMOGRAPHIC MYELOGRAPHY IN THE INVESTIGATION OF CHILDHOOD SCOLIOSIS AND SPINAL DYSRAPHISM

C. I. Rothwell and *W. St. C. Forbes

*Department of Radiology, Manchester Children's Hospital and *Department of Radiology, Hope Hospital, Manchester*

The combined radiological investigations of positive contrast myelography and computed tomographic myelography (CTM) were performed on 53 consecutive children Thirty-eight (72%) of these investigations were performed as a routine pre-operative procedure to identify occult spinal dysraphism in patients with childhood scoliosis, the remainder were because of the "orthopaedic syndrome" (six cases), cervical radiculopathy (three cases), back pain (one case) and patients with clinical findings to suggest spinal dysraphism (five cases). In the 20 patients (38%) with idiopathic scoliosis, there was no case of spinal dysraphism and the CTM provided no additional information to the myelogram. All seven patients with spinal dysraphism were identified and had radiological evidence of spina bifida (five lumbar vertebral abnormalities, one thoracic vertebral abnormality and one case of sacral agenesis). Diastematomyelia was found in four patients, a low tethered cord and lipoma in two patients and a large lipoma in one patient. In all of these cases the myelogram indicated the intraspinal abnormalities; however, the CTM provided more precise anatomical detail. We conclude that CTM is not indicated in the initial pre-operative assessment of idiopathic scoliosis but should be reserved for patients with congenital or complicated scoliosis where the association with dysraphism is well recognised.

### PARASYMPHYSEAL INSUFFICIENCY FRACTURES

A. M. Davies and N. Evans

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We present the clinico-radiological features of 11 patients with a stress fracture through osteopenic bone adjacent to the pubic symphysis (parasymphyseal insufficiency fractures) seen in our department within the last 3 years. Previously 32 cases of this recently recognised condition have been published in the American literature but none in the British. Our group forms the largest individual series so far collected and many similarities with the published cases are apparent. All were post-menopausal women, mean age 68 years Predisposing aetiology included rheumatoid arthritis, steroid therapy, previous hip replacements and radiotherapy. The commonest presenting complaint was chronic hip or groin pain In no case was a significant history of trauma elicited. Radiologically, the fractures initially appeared as a vertical fracture adjacent to the pubic symphysis with disproportionate lysis Subsequently a mixed lytic and sclerotic lesion would develop, mimicking a malignant lesion and slow to show signs of healing. In only six cases did the relevant clinician spot the lesion on the radiographs and in five of these cases the signs were interpreted as those of a malignant lesion. The radiologists came to a similar conclusion in the first two cases of the series, which were duly biopsied. Subsequently, the radiologists confidently diagnosed the remaining nine cases as being insufficiency fractures

Bone scans were performed on six patients and computed tomography of the pelvis on three These were particularly valuable in demonstrating other occult fractures. In retrospect, six cases were shown to have concomitant stress fractures of the sacrum, one of which also had an iliac and a supra-acetabular fracture This association between parasymphyseal and sacral insufficiency fractures has only recently been recognised. The incidence of these fractures can be expected to increase with an aging population. It is important that they are correctly diagnosed if the patients are not to undergo extensive investigations and biopsy for a presumed malignancy.

### CHIMPANZEE HIP?

C. W. Hutton and *I Watt

*Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath and *Department of Radiodiagnosis, Bristol Royal Infirmary*

Joints most often affected by osteoarthritis (OA) are joints that appear to have been subjected most recently to evolutionary change with the development of obligate bipedalism from the knuckle-walking position of hominid ancestors and higher apes Persistence of an ancestral joint configuration inappropriate to present function might predispose to the development of OA. The possibility that OA of the hip may be associated with an acetabular conformation typical of higher apes, a shallow acetabular depth with a vertical and lateral orientation, was investigated by comparing acetabular depth and orientation on radiographs in 150 patients having total hip replacement for OA and 100 controls with radiographs of hips taken during intravenous urography. Acetabular depth was measured as the maximum depth from a line joining the superior acetabular margin to the upper border of the obdurator foramen Acetabular orientation was measured by the angles of the posterior and anterior acetabular margins to a horizontal across the obdurator foramina. The difference between these angles represented the acetabular angle. A small angle reflects a lateral acetabular orientation. There was a significant ($p > 0.05$) reduction in the acetabular depth in OA (18.03 ± 5.18 mm) compared with controls (20.69 ± 4.22 mm). Acetabular orientation was similar in both groups. This suggests acetabular orientation is not a major predisposition in the majority of hips that develop OA However, a plot of acetabular angle against the posterior acetabular angle identified a cluster of five laterally orientated hips that did not occur in controls. All had concentric OA that only occurred in 17% of the patients with OA. These may represent a small subgroup of patients predisposed to OA because of an acetabular configuration more appropriate to a knuckle-walking gait.

### SYNOVIAL CHONDROMATOSIS

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This relatively rare condition is thought to arise when cartilage foci develop by metaplasia in the subsynovial connective tissue of joints, bursae or tendon sheaths. Traditionally, the pathological features have been divided into three stages, comprising purely synovial (I), synovial and loose bodies (II), and loose bodies alone (III) There has been no attempt to correlate these phases with radiological findings nor is there necessarily proof that the disease progresses from Stage I to II or III. It has also been suggested that the presence of synovial chondromatosis promotes degenerative arthritis in the affected joint. A review of 51 cases presenting in the Bristol Bone Tumour Registry demonstrates a heavy preponderance of involvement of the knee joint. However, some 21% of cases are non-articular in site. Stage I disease may frequently be radiologically misinterpreted as non-specific joint swelling or synovitis, although arthrography provides diagnostic information. Even the established Stage II disease may prove difficult to diagnose on plain radiographs as only 88% of cases show calcification. Follow-up suggests that while rim osteophytosis and patello-femoral degenerative arthritis do occur in patients with the disease, there is no loss of hyaline cartilage thickness or other stigmas of osteoarthritis.

### TUMORAL CALCINOSIS: RESPONSE TO PHOSPHATE DEPRIVATION

J. E. Adams and *M. Davies

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Tumoral calcinosis is a rare, genetically determined disorder, usually inherited through an autosomal recessive mode of transmission The condition is characterised by soft-tissue masses of amorphous calcium phosphate which develop in relation to large joints. The aetiology of the disease is uncertain the only consistent biochemical abnormality is hyperphosphataemia, in some patients there is increased production of 1,25-dihydroxycholecalciferol. In the past, treatment usually involved surgical excision of the tumour masses, but these tended to recur. We describe two affected siblings who first developed calcified tumoral masses when they were in their late teens Repeated surgical excisions had proved unsuccessful and had resulted in considerable morbidity (chronic sinus formation in the scars and sciatic nerve damage).

An alternative treatment for the condition is phosphate deprivation, and this was instituted in our patients by the use of oral aluminium hydroxide. The pre-treatment radiographs showed the characteristic features of the disease, with extensive soft-tissue calcification around the hips, shoulders and elbows, and in addition, vascular, intervertebral disc and dural calcification One patient had destruction and dislocation of an elbow and femoral head Within 3 months of starting treatment the tumour masses liquified and were much reduced in size Over the period of observation (18 months), there was dramatic regression of the soft-tissue calcification, although the vascular and disc calcification remained unchanged. Phosphate deprivation offers a simple and effective treatment for tumoral calcinosis

## THE USE OF SONOMAMMOGRAPHY IN ASSESSMENT OF VOLUME CHANGE IN PRIMARY CARCINOMA OF BREAST IN RESPONSE TO ADJUVANT THERAPY

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This paper discusses a simple method of assessing volume change in adjuvant therapy for primary carcinoma of breast, which is currently under trial at Watford General Hospital. Patients are referred to the Ultrasound Department with a clinically detectable lump in the breast before needle biopsy. Patients are scanned in the 45° supine oblique position with an arm extended under the head and the affected side raised A Siemens mechanical 5 MHz sector scanner with a waterbath attachment is used Criteria for diagnosis of breast carcinoma by ultrasound are irregular mass *with* tissue reaction, and sound attenuation Two observers obtain, independently and at the same time, five measurements· longitudinal and transverse scans at the widest diameter, width, depth, height and surface area Then volume = 0 5233 × width × height × depth = $C^3$. The patients are then divided into two groups according to the referring team. Group A (A.G.H. and K B). following a needle biopsy to confirm the diagnosis, the surgical specimen of "the whole tumour" is measured in the laboratory to correlate the reading with ultrasound. Group B (S C and R. A ). following the result of the needle biopsy, tamoxifen therapy is started—40 mg b.d is given for 1 week followed by 20 mg b d. thereafter Treatment is continued until there is either evidence of tumour progression on ultrasound or clinically, or no further regression At this stage (often more than 6 months later), a lumpectomy is carried out, followed by post-operative irradiation, Tamoxifen is continued in Group B for a further 2 years before review Patients in this group are scanned once every 2 weeks and the volume is plotted graphically. The object of the trial is to identify by volume changes the growth-rate response to therapy, to identify the marker to readjust therapy, and to introduce a simple, accurate technique to assess volume changes objectively.

## TRAINING IN MAMMOGRAPHIC INTERPRETATION

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As a prelude to computer-assisted diagnosis in mammography, we have previously demonstrated that good mammographic interpretation is possible when a small number of particular radiographic features are reliably interpreted by the observer. On a series of 500 cases proven at biopsy, this approach correctly identified some 78% of malignant and 88% of benign cases While this performance is not as good as that of an expert radiologist in identifying malignant disease it does suggest a worthwhile approach to training in mammographic interpretation, particularly for mammographic screening. The present study set out to determine whether it was possible to train naïve subjects to identify relevant features on mammograms. Medical students were randomly allocated to either an experimental or a control group. The performance of both groups was examined on four separate occasions over several days, when subjects were tested on a series of 100 oblique-view mammograms. Between each test session both groups were shown a series of additional mammograms and asked to indicate whether they were benign or malignant. Both groups received feedback about the correctness of their response, but in addition the experimental group was presented with a description of the film in terms of the particular radiological features previously identified as important Data were analysed using signal detection theory. Results demonstrated that while the control subjects improved their performance this did not alter much after the second test session In contrast, the performance of the experimental group continued to improve until they identified 75% of the malignant cases. Implications of these results for training in mammography are discussed.

## DOPPLER ULTRASONOGRAPHY OF AN EXPERIMENTAL SOFT-TISSUE TUMOUR: THE EFFECTS OF A VASOCONSTRICTOR

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Previous studies have demonstrated the production of Doppler signals by malignant tumours and carcinoma of the female breast has been widely studied (Burns et al, 1982) We have used a VX2 sarcoma implanted in the pinna of a rabbit to study the effects of vasoconstriction on these signals Twelve rabbits were examined using a 10 MHz continuous-wave Doppler transducer Recordings were made from the tumour and the central artery of the pinna in the basal state and during infusion of angiotensin II The Doppler information was processed using a commercially available spectrum analyser and an Apple II microcomputer. The maximum frequency envelope was defined and the maximum systolic (MAX), maximum diastolic (MIN) and time-averaged mean (TAM) frequency shifts were derived. The ratios MAX/TAM and MIN/TAM were calculated and the results (mean and range) are shown in Table I.

TABLE I

| | Basal | | Vasoconstricted | |
|---|---|---|---|---|
| | Tumour | Artery | Tumour | Artery |
| MAX/TAM | 3 85 (3 55–4 85) | 3 25 (2 63–4 23) | 3 58 (3 18–4 43) | 2 72 (2 48–2 87) |
| MIN/TAM | 1 99 (1 74–2 30) | 1 59 (1 44–1 70) | 2 09 (1 83–2 51) | 1 67 (1 58–1 74) |

Our conclusions are that the use of a vasoconstrictor modifies the signals from both the tumour and the artery and that both the MIN/TAM and MAX/TAM ratios following vasoconstriction could be effective discriminators between the two signal sources

### REFERENCE

Burns, P. N., Halliwell, M., Wells, P. N. T. & Webb, A. J., 1982 Ultrasonic Doppler studies of the breast. *Ultrasound in Medicine and Biology, 8,* 127–143

## Agents for Image Enhancement

**Chairman: Professor I. Isherwood**

The science of X-ray contrast media, by P Dawson
Clinical indications and contra-indications for the use of ionic and non-ionic contrast media, by P Davies
Complications with X-ray contrast media, by G. Ansell
Contrast agents for enhancement of magnetic resonance images, by L D Hall
Preliminary results with an ultrasound contrast agent, by Th. Fritzsch, M Schartl and J Siegert
Contrast media: financial and ethical considerations, by R. G. Grainger

### THE SCIENCE OF X-RAY CONTRAST MEDIA

P Dawson

*Department of Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London*

Without the availability of good and safe contrast agents, diagnostic radiology would not have come to occupy the important place it currently does in modern medicine. In one sense these contrast agents are now no more than reliable tools of the radiologist's trade and it is therefore not at all surprising that their detailed chemistry and pharmacology is not of any great interest to most practical radiologists. Nevertheless, they represent a fascinating and many-faceted field of study. In this presentation, the physics, chemistry and pharmacology of contrast agents are discussed against a historical back-cloth. The story of their evolution is itself fascinating but on closer study also, surprisingly, provides useful insights into the mechanisms of contrast-agent toxicity

### CLINICAL INDICATIONS AND CONTRA-INDICATIONS FOR THE USE OF IONIC AND NON-IONIC CONTRAST MEDIA

Peter Davies

*X-ray Department, Nottingham City Hospital*

Many beliefs about reactions to contrast media are based on theory rather than clinical study. There are some surprising observations. fast injections and large doses are as safe as slow injections and small doses, pre-testing and prophylaxis are valueless, most severe reactions are unpredictable and do not recur on challenge; as the toxicity of contrast media has declined so that death rate has risen Delayed reactions are common and more frequent than the corresponding acute reactions, which do not predict them. Only small differences in rates of reactions have been demonstrated for the ionic and non-ionic media. The patient is the most important determinant of reactions. Important risk factors are cardiac status and mental condition Patients at risk should be counselled and managed according to the scheme outlined by Lalli

The dose of contrast medium should be restricted to that necessary to produce an adequate examination; for urography this is 50 ml of a sodium ionic medium containing 300 mg/ml of iodine (15 g). It should not be necessary to exceed a dose of 84 g, which should be equally safe for ionic and non-ionic media. Low-osmolar contrast media are more comfortable for the patient and cause less movement; they are therefore indicated for angiography, although their advantages for intravenous work appear negligible

### COMPLICATIONS WITH X-RAY CONTRAST MEDIA

G. Ansell

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Minor and moderate reactions to contrast media are not infrequent, but severe and fatal reactions are rare, requiring large surveys to provide sufficient data for analysis. The reported incidence for severe reactions varies from approximately one in 4000 to one in 1000 Reported mortality rates vary from one in 93000 to one in 15000 The majority of severe and fatal reactions occur within 20 min of the injection. Factors influencing the risk of severe reactions include a history of previous reactions, allergy, particularly asthma, heart disease and age. Dose is also relevant and there may be ethnic variations Some delayed reactions may go undiagnosed and their frequency has probably been underestimated in the past. In susceptible patients, there may be cardiac, renal or neural complications arising from constrast-medium toxicity Preliminary studies of non-ionic media suggest that the incidence of reactions is reduced but severe reactions may still occur Corticosteroid prophylaxis should be considered in certain high-risk cases and there must be adequate provision for the treatment of reactions

### CONTRAST AGENTS FOR ENHANCEMENT OF MAGNETIC RESONANCE IMAGES

L. D. Hall

*Laboratory for Medical Chemistry, University of Cambridge Clinical School, Addenbrooke's Hospital, Cambridge*

Much of the diagnostic utility of magnetic resonance imaging depends on variations of the relaxation rates of water protons (because of endogenous variations of cellular environment in different organs) and between normal and pathological tissues Nevertheless, there are a number of circumstances where this endogenous contrast is insufficient even for unequivocal anatomical distinction, and other circumstances where enhanced contrast would facilitate tissue characterisation Following the precedent of X-ray imaging, it has been suggested that in both these circumstances image contrast media should be used, and this approach has already been documented for a water-soluble complex of the rare-earth element gadolinium. In principle, any substance which can influence the magnetic resonance properties of water can be used as a magnetic resonance contrast medium and it is not difficult to contemplate the delightful prospect of pathology-specific contrast media In practice, however, the field is narrowed by the need for patient safety, by the wish to avoid unnecessary complications, and by the difficulties of obtaining regulatory permission for what might be classified as a "new pharmaceutical" This presentation provides a general overview of past practice in this area and attempts to identify future options.

### PRELIMINARY RESULTS WITH AN ULTRASOUND CONTRAST AGENT

Th. Fritzsch, *M. Schartl and J. Siegert

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Contrast agents for diagnostic ultrasound have been known for nearly 20 years. However, since there is still no commercially available compound, all the contrast agents used today have to be produced by hand, and so lack reproducibility, safety and homogeneity in contrast effects. SH U 454 is a new, standardised echo-contrast agent which consists of a suspension of specially treated galactose microparticles (50% < 2 $\mu$m). After injection these microparticles dissolve and release tiny gas bubbles (97% < 7 $\mu$m) which opacify the blood. Because they have a short half-life, the bubbles cannot cross the lungs.

In cardiology, more than 500 patients with congenital or acquired right heart diseases were investigated Atrial and ventricular septal defects were easily identified, as well as tricuspid insufficiencies In addition, use of a contrast agent was beneficial for depicting complex anatomical situations Tolerance was good and the only side-effect observed, and only in some patients, was a feeling of warmth due to the osmolality of the agent

Employment of image-processing methods such as digital subtraction echocardiography seems to offer further advantages in quantification SH U 454 seems to offer advantages in areas besides cardiology, *e.g.* urology, gynaecology and gastroenterology Clinical trials are under discussion Other echo-contrast agents with different characteristics are under development. Thus, the use of a standardised contrast agent with defined characteristics seems to enlarge the diagnostic potential of sonography

### CONTRAST MEDIA: FINANCIAL AND ETHICAL CONSIDERATIONS

Ronald G. Grainger

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The brilliant synthesis and clinical introduction of contrast media of reduced osmolality and toxicity have not been followed by their full clinical application because of their high cost (involving a factor of five in the UK). In the UK in 1986, 33% of contrast medium used was low-osmolar, generally used in accordance with the College guidelines, increasing cost by £6 million per annum. A further £12 million per annum would be necessary for low-osmolar contrast media to be used solely The advantages would be more comfortable injections and fewer minor, serious and probably fatal reactions. But this increased radiological expenditure must be justified against the needs for improved imaging equipment and an increased radiological establishment.

The cost of both high- and low-osmolar media and their differential varies considerably in different countries (by a factor of five). Differing financial allocations and methods of medical financing, medico-legal aspects as well as clinical considerations will influence the inevitable and commendable drift towards the safer but more expensive low-osmolar media There will be substantial improvement in patient comfort and safety but will this always be the correct decision?

## Clinical: Gastrointestinal and Abdominal

**Chairman: Professor G. Whitehouse**

Magnetic resonance imaging of parotid tumours, by F W. Smith, K. McLay, C W Rayner and A. Law

Swallowing disorders in the elderly: a review of current concepts and videofluoroscopic demonstration of common abnormalities, by M S. M Alexander

The videofluoroscopic swallow: a combined approach in head and neck cancer patients with dysphagia, by M. S. M Alexander

Endoscopic ultrasonography in the investigation of oesophageal carcinoma: preliminary observations, by P J. Shorvon, R. A. Frost and W R Lees

The cup overfloweth a radiological artefact? By A Booth and J. Virjee

Gastric diverticula, by C Davies, A. Longstaff and J. Virjee

Primary tumours of the duodenum, by N C G. Bathurst and J. Virjee

Histiocytoma of the jejunum, by H.-J Maurer

Intestinal malignancy associated with Crohn's disease, by M. Morse and J Virjee

The differentiation of benign and malignant colonic strictures in diverticular disease, by J. Kabala and J. Virjee

### MAGNETIC RESONANCE IMAGING OF PAROTID TUMOURS

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Thirty-two patients with clinically suspected disease of the parotid gland have been studied by magnetic resonance imaging (MRI) and X-ray computed tomography (CT). In all cases detailed clinical, operative and histological findings have been compared with the MRI observations. Of the 32 patients studied, three had normal parotid glands, 19 had benign disease, and 10 had malignant tumours of one or other parotid gland Both MRI and CT demonstrated all lesions present. However, it was not always possible to differentiate the type of tumour from the appearances on MRI and specific $T_1$ measurements. Gross malignant disease was recognisable by the destruction of surrounding normal tissues. Less severe malignant disease was not always differentiated from abscess and in one case the appearances were the same as those seen in pleomorphic adenomas The main advantages of MRI in this region are the ability to perform sections in the axial and coronal planes and the clarity with which the retromandibular vessels, which lie in close association with the facial nerve, are seen. The recognition of these vessels and their relationship to any mass is of prime importance when planning surgery in this region. While MRI is not specific for disease diagnosis, it has been found to be very sensitive in the detection of parotid masses and in demonstrating their relationship to the facial nerve and mandible.

## SWALLOWING DISORDERS IN THE ELDERLY: A REVIEW OF CURRENT CONCEPTS AND VIDEOFLUOROSCOPIC DEMONSTRATION OF COMMON ABNORMALITIES

M. S. M. Alexander

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The current literature on swallowing disorders in the elderly is reviewed. The videofluoroscopic swallow technique, including quantitative analysis, is described, with modifications for the elderly. Demonstration of normal anatomy is illustrated with a normal videoswallow. Videofilm, with commentary, of the major swallowing disorders is shown, including Parkinson's disease, motor neurone disease, oculopharyngeal myopathy, myasthenia gravis, cervical osteophyte and pseudobulbar palsy The role of the technique in diagnosis and management of these conditions and areas for future study are discussed.

## THE VIDEOFLUOROSCOPIC SWALLOW: A COMBINED APPROACH IN HEAD AND NECK CANCER PATIENTS WITH DYSPHAGIA

M. S. M. Alexander

*Department of Radiology, Hammersmith Hospital, London*

The method of assessment in the Dysphagia Clinic at Hammersmith Hospital is described. The patient is examined and assessed by the speech therapist and the radiologist then performs a modified barium swallow to examine fully the oral and pharyngeal phase of the swallowing mechanism. The details of the fluoroscopic technique are described, with diagrams of normal anatomy and viewing of a normal videoswallow. A specially designed combined report is then demonstrated, with recommendations for future management included in it The approach is demonstrated in 16 patients treated with radiotherapy and/or surgery for head and neck cancer The findings and recommendations for management are summarised. Videofilm of selected patients with commentary is shown to illustrate the range of abnormalities found. Patients compensate for anatomical defects by changing head posture and varying dietary consistency Symptoms of dysphagia are shown to arise either because intercurrent infections, such as *Candida*, cause oedema and further anatomical distortion leading to decompensation or, in radiotherapy patients, because of a process of fibrosis with similar though less acute decompensation. This decompensation then leads to the hazards of aspiration and malnutrition, which are of primary concern in management. In addition, the value of demonstrating a successful and well compensated swallowing reflex to an anxious patient is stressed.

## ENDOSCOPIC ULTRASONOGRAPHY IN THE INVESTIGATION OF OESOPHAGEAL CARCINOMA: PRELIMINARY OBSERVATIONS

P. J. Shorvon, R. A. Frost and W. R. Lees

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Oesophageal carcinoma has an appalling prognosis, with a 5-year survival of approximately 4% Few lesions are found to be resectable. Even resection, with a high peri-operative morbidity and mortality, is rarely curative Many palliative therapies exist, but there is need for an imaging modality to select the few patients who may benefit from resection Computed tomography (CT) is the best established method, but its accuracy is low. Endoscopic ultrasonography (EUS), utilising a high-frequency ultrasound transducer incorporated into the tip of a fibre-optic endoscope, produces high-resolution images of the oesophageal wall and contiguous organs. The oesophageal wall is displayed as three layers, with an echo-poor layer (muscularis propria) sandwiched between two echo-dense layers. Extension of tumour through the muscularis propria is seen as thickening of the echo-poor layer with destruction of the outer echo-dense layer (adventitia). Deeper invasion into the mediastinal fat, involvement of adjacent organs (*e.g.* pericardium and aorta) and lymph-node enlargement are well visualised.

Eighteen patients with oesophageal carcinoma proven by biopsy (one carcinoma *in situ*) underwent EUS using an Olympus instrument (7.5 MHz mechanical sector scanner). In 12 patients the instrument traversed the entire carcinoma, whereas in six it was impossible to pass beyond the proximal stricture Unresectability was diagnosed in 11 of the 18 on the basis of deep extension into the mediastinum or invasion of contiguous organs. The patient with carcinoma *in situ* showed no evidence of invasion. Of the remaining six patients, three underwent resection and the EUS findings were confirmed. The tumours often were demonstrated to extend submucosally up to 6 cm above the endoscopic visual extent In five of the six patients in whom the endoscope could not be passed through the stricture, mediastinal invasion or lymph-node involvement was demonstrated at the upper aspect of the tumour, Endoscopic ultrasonography provided more precise information than CT.

## THE CUP OVERFLOWETH: A RADIOLOGICAL ARTEFACT?

A. Booth and J. Virjee

*Department of Radiodiagnosis, Bristol Royal Infirmary*

The presence of a "cup and spill" (cascade) stomach is frequently seen during double-contrast barium meal examinations and has been considerd previously to represent a variant of gastric volvulus or normality We have noted a relatively high incidence of this appearance, especially in young patients presenting with the symptom complex of epigastric pain beginning immediately after food. In order to evaluate the significance of the radiological appearance we have studied the oesophagogastric flow of barium and correlated this with the onset of symptoms. We have also studied the relief of both the anatomical appearances and symptoms on forward bending. We have evaluated 40 such patients and have compared them with a matched cohort of 40 patients with the same symptom complex but who have no anatomical variant. We have conclusively shown that the cup and spill appearance is a radiological artefact with no significant element of volvulus and is almost certainly seen more frequently with the increased use of a routine hypotonic agent and high-density barium suspension.

## GASTRIC DIVERTICULA

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**Department of Radiodiagnosis, Frenchay Hospital, Bristol*

True gastric diverticula are uncommon. They occur in approximately one in 600 barium examinations and show a prevalence which ranges from 0.1% to as high as 2 6% in some post-mortem studies. Three quarters of these diverticula arise in an identical juxta-cardia position and have a typical radiographic appearance. Patients are invariably asymptomatic but occasionally present with complications We report five patients in whom fundal diverticula were diagnosed by radiographic studies Two of these patients presented with dramatic symptoms directly related to the diverticula. In three the diverticula were apparently incidental findings and the abdominal symptoms were attributed to other causes. In this latter group, endoscopy was undertaken and the diverticula were overlooked in two cases and misinterpreted in one In one patient a discrepancy between the barium and the endoscopic findings led to some delay in diagnosis of a carcinoma. We illustrate these five cases and review the subject of gastric diverticula.

## PRIMARY TUMOURS OF THE DUODENUM

N. C. G. Bathurst and J. Virjee

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Primary tumours of the duodenum, excluding ampullary carcinoma, are relatively rare, representing 0.3% of all gastrointestinal carcinomas. To obtain optimal mucosal detail demands the routine use of a hypotonic double-contrast delineation of the duodenum The ease with which this is achieved and the confidence it engenders is demonstrated Twenty-two cases of primary benign and malignant tumours of the duodenum (excluding ampullary carcinoma) are presented. The radiological features and their importance, particularly when compared with the presenting clinical features, which are often non-specific, are discussed The ability of barium studies to detect these lesions is compared with that of endoscopy, particularly in relation to lesions of the third and fourth parts of the duodenum which invariably are not examined or are inaccessible endoscopically.

## HISTIOCYTOMA OF THE JEJUNUM

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Malignant lymphomas represent a very small proportion of tumours of the small bowel Diagnosis from symptoms is often very difficult and so further diagnostic procedures are often inappropriate This paper describes the case of a 46-year-old man with arterial stenosis and symptoms of vomiting and weight loss. Two months after presentation gastroscopy showed a ventricular neurinoma and duodenal sprue As symptoms continued, digital subtraction angiography was performed to exclude abdominal arterial obstructions. However, a highly vascular tumour was found in the right upper abdomen Small-bowel enema showed the tumour, probably a carcinoma, obstructing the upper jejunum This was apparently confirmed at surgery Histologically, however, the lesion proved to be a non-Hodgkin's lymphoma and immunological investigations confirmed it to be a histiocytoma The correlation between histiocytoma and sprue is discussed along with methods of diagnosis.

## INTESTINAL MALIGNANCY ASSOCIATED WITH CROHN'S DISEASE

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The association of inflammatory bowel disease and intestinal malignancy is well recognised, particularly so with regard to ulcerative colitis. Crohn's-disease-associated intestinal malignancy (CDAIM) is, however, less well documented and the factors placing a particular patient at risk are less clear than in ulcerative colitis We have examined five previously unreported cases of CDAIM and reviewed the literature, with particular respect to the radiographic findings, in an attempt to discover signs which may suggest the development of malignancy Radiographic evidence of disease progression, such as the development of masses, fistulae, strictures or obstruction, particularly when combined with a recrudescence of symptoms following a relatively quiescent period, is highly suspicious In view of the associated high mortality, a policy with an aggressive investigative approach is warranted in these patients.

## THE DIFFERENTIATION OF BENIGN AND MALIGNANT COLONIC STRICTURES IN DIVERTICULAR DISEASE

J. Kabala and J. Virjee

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A survey of colonic strictures on double-contrast barium enemas (DCBEs) performed in the Bristol Royal Infirmary (under routine conditions) demonstrated a level of accuracy of 92% in determining the nature of the strictures However, the usefulness of a DCBE in differentiating "benign" from "malignant" strictures, in the presence of diverticular disease, is still disputed with quite poor reliability sometimes being suggested. Radiological features of benign strictures (mucosal integrity, length, soft-tissue mass, adjacent "zig-zag" mucosa) and malignant strictures (rolled edge, abrupt transition to normal bowel, presence of polyps) have been alluded to in the past, but without describing the frequency with which these signs occur. In order to determine the relative value of these signs the DCBEs of 80 patients with diverticular disease and associated proven benign (50%) or malignant (50%) strictures were examined. Clinical parameters such as the white cell count and the presence of a palpable mass were also assessed in the differentiation between these two conditions, which we believe can be achieved *radiographically* in a very high percentage of cases

AUGUST 1987

*Proceedings of The British Institute of Radiology*

# Posters. Nuclear Medicine and Ultrasound

**Chairman: Dr A. Smith**

An evaluation of the energy correction procedure on a digital gamma camera, by S J. Chittenden

Use of a personal computer to measure the spatial resolution of a gamma camera, by A. L. Walker, H. M Norwood, A. Parkin and A. J Hall

A general software system for the handling of medical images, by J. S Fleming, A J. Britten, G M. Blake, J. Gray and P. J. Howlett

Imaging inflammation with technetium-99m-HMPAO-labelled white cells, by M E. Roddie, A. M. Peters, B. L. Henderson, S. Osman, H J. Danpure and J P Lavender

Comparison of white cells labelled with technetium-99m-HMPAO and indium 111 for imaging inflammation, by M E. Roddie, A M Peters, B L. Henderson, S Osman, H J. Danpure and J. P. Lavender

Investigation of the factors affecting the measurement of paediatric aortic and pulmonary flow using a flow rig simulation, by F J Soul, T K Hames, V. Thomas and R J Bacon

## AN EVALUATION OF THE ENERGY CORRECTION PROCEDURE ON A DIGITAL GAMMA CAMERA

S. J. Chittenden

*Physics Department, Royal Marsden Hospital, Sutton, Surrey*

A uniform flood source placed in front of a gamma camera is unlikely to produce a uniform image. Two possible causes of non-uniformity are the variation in sensitivity between photomultiplier tubes across the camera face and their variation in response to photons of identical energy, depending on whether a photon falls directly over a photomultiplier tube or between two tubes. The resulting variations in energy signal detected at different positions across the camera face can be measured and removed by applying appropriate values from an energy correction matrix to all data entering the camera A uniform flood source imaged with the correction matrix applied should then result in a uniform image (ignoring other possible causes of non-uniformity)

Radionuclides of different peak energies require different energy correction matrices On the IGE Starcam system, corrections for any radionuclide may be derived, stored on the computer and applied to appropriate images as they are acquired The procedure used on the Starcam to generate energy correction matrices has been evaluated. In particular, the reproducibility of the procedure (which is carried out monthly) has been investigated and the effects of applying various correction matrices to incoming flood data have been compared with results obtained when no correction has been applied. The non-uniformity of the images has been calculated using the method recommended by the National Electrical Manufacturers Association Results obtained to date from a Starcam 400AT camera show that it is possible to achieve integral and differential non-uniformity of less than 2.5% and 2% respectively for the central field of view of the camera, and 8% and 6% respectively for the useful field of view. These values can be achieved for any radionuclide within the normal range of use of the camera, providing the appropriate correction matrix is applied

## USE OF A PERSONAL COMPUTER TO MEASURE THE SPATIAL RESOLUTION OF A GAMMA CAMERA

A. L. Walker, H. M. Norwood, A. Parkin and A. J. Hall

*Medical Physics Department, St James' University Hospital, Leeds*

A standard Apple IIe microcomputer has been converted to a versatile multichannel analyser (MCA) by adding an interface card and 10-bit analog-to-digital convertor (NMESS Ltd) The MCA, which normally measures energy spectra, can easily be changed to measure gamma-camera spatial resolution. The $X$ or $Y$ output from a gamma camera, suitably amplified, is applied to the pulse input of the MCA, which can measure the position of an event in the crystal to a resolution of better than 0.2 mm. Construction of a suitable line source enables the spatial resolution (FWHM) of the camera to be determined. Typical results for three gamma cameras are presented. Results for one of these cameras are shown before and after head overhaul to replace faulty optical grease. This is a cheap, readily applicable method for measuring gamma-camera spatial resolution following servicing, or during acceptance testing of a new camera.

## A GENERAL SOFTWARE SYSTEM FOR THE HANDLING OF MEDICAL IMAGES

J. S. Fleming, A. J. Britten, G. M. Blake, J. Gray and *P. J. Howlett

*Medical Physics Department, Southampton General Hospital and *Medical Physics Department, St Mary's Hospital, Portsmouth*

A software system, PICS (portable imaging computer software), which is designed for handling and processing a variety of types of medical image, is described It has been developed to satisfy the following criteria

(a) The package should be portable between different hardware with minimal alteration to the software
(b) There should be a simple operator interface to enable use by inexperienced users.
(c) The programming environment should enable simple integration of new data handling protocols to allow their rapid inclusion in clinical routine.

The requirement of portability is met by writing the software in FORTRAN with structured subroutine organisation The operator–program interface is simplified by the use of menu-driven commands together with a type-ahead facility for more experienced users. The last requirement has been met by ensuring that the software modules are kept as general as possible in application to facilitate their use by the whole programming team.

The software is currently implemented on a VAX 11–730 computer with Sigmex A7000 processor. This system is capable of handling images up to 512 × 512 pixels. The software has basic image handling facilities and contains a comprehensive set of nuclear medicine clinical protocols The operation of the software is briefly described and examples of specific routines given, including automatic edge detection, renogram mean transit time imaging, and image superimposition Image transfer is available from the following sources: nuclear medicine—Link MAPS, serial line and magnetic tape, and IGE star, magnetic tape, computed tomography—Siemens, floppy disc, and Picker, magnetic tape A video digitiser is currently being installed which will enable digitisation of radiographs and ultrasound images This system will provide a hospital with a central digital image handling resource, enabling investigation of the value of digital image processing in potential clinical applications.

## IMAGING INFLAMMATION WITH TECHNETIUM-99m-HMPAO-LABELLED WHITE CELLS

M. E. Roddie, A. M. Peters, B. L. Henderson, *S. Osman, *H. J. Danpure and J. P. Lavender

*Department of Diagnostic Radiology and *MRC Cyclotron Unit, Hammersmith Hospital, London*

The use of $^{111}$In-labelled leucocytes in the detection of inflammation is established. Because of convenience, radiation dose and image resolution, $^{99}$Tc$^{m}$ would be preferred as a label. The lipid-soluble complex that $^{99}$Tc$^{m}$ forms with HMPAO rapidly enters leucocytes *in vitro* with a greater efficacy and stability for granulocytes than other cells. Mixed leucocytes were separated from 100 ml of blood anticoagulated with acid citrate dextrose and resuspended in 0.5 ml plasma After adding 5 ml of $^{99}$Tc$^{m}$ eluate to a vial of HMPAO, 4 5 ml of the complex was added to the leucocytes After 10 min, 10 ml of cell-free plasma was added, the cells repelleted (100 g) and the supernatant discarded The cells were reinjected into 5 ml cell-free plasma Ninety per cent of the $^{99}$Tc$^{m}$ complexed with HMPAO and the cells were labelled with an efficiency of 47%.

We have studied 50 patients, 14 with suspected inflammatory bowel disease (IBD), 10 with pyrexia of unknown origin (PUO), 11 with bone sepsis, two with myocardial infarction, two with bronchiectasis and 11 with intra-abdominal sepsis. Three of the last group were known to have IBD. The patients were imaged at 15–60 min, 4 h and 24 h. Urinary activity was seen throughout and colonic activity at 24 h in all patients. In five patients, gallbladder activity was seen. Otherwise the normal distribution of activity was similar to that with $^{111}$In leucocytes Positive scans were seen after 4 h in 12 of the 14 patients referred with IBD, one with PUO, five with bone sepsis, one with myocardial infarction, two with bronchiectasis and nine with intraabdominal sepsis. Sensitivity was 96% and overall accuracy 92%. Because of normal excretion of this complex via bowel, difficulty was anticipated in diagnosing IBD. However, in all but two of the 15 patients with IBD, bowel activity was seen within 60 min The other two with Behçet's syndrome and Whipple's disease had intense activity at 4 h Only four patients without IBD had bowel activity at 4 h, and this was faint. The technique accurately diagnoses inflammation, including IBD, within 4 h of injection

## COMPARISON OF WHITE CELLS LABELLED WITH TECHNETIUM-99m-HMPAO AND INDIUM 111 FOR IMAGING INFLAMMATION

M E. Roddie, A. M. Peters, B. L. Henderson, *S Osman, *H. J. Danpure and J P. Lavender

*Department of Diagnostic Radiology and *MRC Cyclotron Unit, Hammersmith Hospital, London*

Indium-111-labelled white cells are well established as a means of detecting inflammation Technetium 99m forms a lipid-soluble complex with HMPAO which binds to leucocytes *in vitro* with a greater efficacy and stability for granulocytes than other blood cells. Mixed leucocytes were separated from 100 ml of fresh venous blood anticoagulated with acid citrate dextrose and, after centrifugation, were resuspended in 5 ml of phosphate-buffered saline and 5 ml of $^{99}$Tc$^{m}$-HMPAO complex was added After 10 min, 10 ml of cell-free plasma was added, the cells repelleted and resuspended, before injection, in a further 5 ml of cell-free plasma Also, "pure" granulocytes were isolated from anticoagulated fresh venous blood and labelled in 90% plasma with $^{111}$In-tropolonate

Eleven patients were imaged using $^{99}$Tc$^{m}$-HMPAO-labelled white cells and re-imaged 48 h later using $^{111}$In-labelled cells. They were imaged at 4 h and 24 h and the technetium scans were also taken at 15–60 min Six patients with inflammatory bowel disease showed intense migration of cells to bowel by 30 min with technetium scanning and by 4 h with both methods. Technetium scanning was more sensitive in detecting the extent of disease in two patients, indium scanning was more sensitive in one patient and the sensitivity was similar in the remaining three The other five patients included two patients with Behçet's disease and two patients with intra-abdominal sepsis. There was no discrepancy between scans in this group. In the last case, with an infected femoral nail, diagnosis was negative with indium scanning and positive with technetium. The two patients with Behçet's disease affecting the gastrointestinal tract showed intense migration to bowel at 4 h but none at 30 min, and there was no difference in the extent of disease detected by either method. Our initial experience suggests that $^{99}$T$^{m}$-HMPAO-labelled leucocytes are as good at imaging inflammation as $^{111}$In-labelled leucocytes.

## INVESTIGATION OF THE FACTORS AFFECTING THE MEASUREMENT OF PAEDIATRIC AORTIC AND PULMONARY FLOW USING A FLOW RIG SIMULATION

F. J. Soul, T. K. Hames, *V. Thomas and †R. J. Bacon

*Departments of Medical Physics, *Anaesthetics and †Medical Engineering, Southampton General Hospital*

The confident non-invasive measurement of blood flow using ultrasound has been attempted by numerous workers In order to evaluate the technique of duplex scanning and its application to the problem of non-invasive assessment of aortic and pulmonary blood flow in a paediatric population, we attempted an *in-vitro* simulation of these flow conditions This allowed us to perform a detailed assessment of the particular ultrasound system used in a parallel clinical study (Toshiba Medical). The factors which have been incorporated in the design of the apparatus include a range of tube diameters, an aortic-"like" waveform, laminar flow, variable downstream peripheral resistance, compliance factor and viscosity of the medium. The ultrasound-probe beam characteristics and sample volume size and shape were also measured Five tubes of diameter 9–20 mm were used to compare, in each tube, a range of flow values from 35 ml to 70 ml per stroke. The flow values were measured by both "bucket and stopwatch" and duplex scanning for both steady and pulsatile flow conditions. The results are presented as correlations between the direct and non-invasive assessment of flow measurement, with a discussion of both the reliability and variability in measurements made with a conventional duplex scanner.

*Proceedings of The British Institute of Radiology*

# Posters. Physics, Radiation Protection and Management

**Chairman: Mr M. Fitzgerald**

A sensitometric investigation of film and xeroradiographic dental radiography, by K. Faulkner, N. A. Farrow and J. Hutton
Development of a digital radiographic technique to measure bone mineral in neonates, by D. J. Hawkes, A. Theodoridou, M. Doran, N McIntosh, A. Lyon and J. E Williams
Measurements of slice dose profiles in computed tomography scanning, by K. Faulkner and D. J. Rawlings
The radiological risks from X-ray examinations and nuclear medicine procedures, by B. F. Wall and P. C. Shrimpton
A stable beam calibration system, by D. Gifford, T. J. Godden and D. Kear
Quality assurance procedures in external-beam radiotherapy at The London Hospital, by R. A. Lake, A. K Morgan and S C. Klevenhagen
Contamination monitoring of the public following Chernobyl, by P. P Dendy, R. Massoumi, K. E. Palmer and K. F Szaz
Changes in the pattern of referrals to the radiology department by clinical specialty, by F A. Paris and W Hull
Workload in a department of diagnostic imaging, by F. A Paris and W. Hull
Teleradiology. Image transmission via the standard telephone networks, with image storage and recovery systems, by R. Atkinson and C. Redman

## A SENSITOMETRIC INVESTIGATION OF FILM AND XERORADIOGRAPHIC DENTAL RADIOGRAPHY

K. Faulkner, N. A. Farrow and *J. Hutton

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Characteristic curves were produced for four types of conventional dental film: Kodak Ektaspeed EP21, Kodak Ultraspeed DF58, Agfa Softopack Dentos M2 and Hanshin QD film The Hanshin QD film has been recently introduced and has the advantage that it may be processed conventionally or instantly within its own film envelope. It was deduced from these characteristic curves that the E-speed film was considerably more sensitive than the other films whilst having a contrast and latitude similar to both the Agfa and Kodak D-speed films. The Hanshin QD film performed very poorly in comparison with the D- and E-speed films as the contrast and sensitivity were lower; however, its performance was better when processed in its own packet An assessment of the contrast and latitude of each imaging system, with the exception of Hanshin film, on anthropomorphic phantoms was made. The reflection densitometry results from the xeroradiographic images indicated that the large-area contrast changed with the adjustment of the xeroradiographic processor. It is difficult to assess the value of the change in contrast as the edge-enhancement effect will have a crucial role to play in the visualisation of contrast in the clinical practice.

## DEVELOPMENT OF A DIGITAL RADIOGRAPHIC TECHNIQUE TO MEASURE BONE MINERAL IN NEONATES

D. J. Hawkes, A. Theodoridou, M. Doran, *N. McIntosh, *A. Lyon and †J. E. Williams

*Departments of Medical Physics and Bio-Engineering and †Radiology, St George's Hospital, and *Child Health, St George's Hospital Medical School, London*

Generalised osteopenia and rickets of prematurity are becoming increasingly common as more premature infants are surviving the neonatal period. Classic radiographic signs of rickets may appear too late to influence management effectively and biochemical assays are often misleading. Photon absorptiometry has a high potential accuracy while delivering a low radiation dose, but available commercial equipment cannot be used on infants confined to an incubator. A technique for the quantification of bone mineral content (BMC) has been developed which uses a mobile X-ray unit and an image analysis computer. X-ray films are taken at 40 kV and 120 kV of the lower arm or lower leg The limb is immobilised in a specially designed holder which incorporates a perspex and aluminium step-wedge. After digitisation and careful densitometric calibration using the images of the step-wedges, dual-energy analysis yields measurements of BMC in units of mass of bone mineral per unit area of the image. This measurement may be integrated over the image of a particular bone to yield total BMC for that bone or the results may be expressed as BMC per unit length of the shaft. Results of studies on the limbs of small animals and initial work on neonates are presented. The whole-body effective dose equivalent received by an infant is estimated to be 0.4 μSv per investigation, which is about 40 times less than for an X-ray examination of the chest of a neonate.

## MEASUREMENTS OF SLICE DOSE PROFILES IN COMPUTED TOMOGRAPHY SCANNING

K. Faulkner and D. J. Rawlings

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Slice dose profile measurements have been made at the isocentre of computed tomography (CT) scanners using thermoluminescent dosimetry (TLD). The TLD probes consisted of long thin cylinders of Teflon (outside diameter 1.5 mm) into which lithium fluoride has been loaded. These TLD probes were read out on a therados TLD-20 reader and have a read-out distance of 1 mm, which means that they are particularly useful for performing slice dose profile measurements on CT scanners with narrow slice widths. The radiation dose at the isocentre for multiple slices may be deduced from these slice dose profiles, and they were compared with results obtained using an ionisation chamber with a long narrow sensitive volume. On certain CT scanners with suitable software algorithms, it is possible to produce three-dimensional anatomical images from a series of contiguous narrow slice width CT scans. The radiation dose to a number of critical organs may be deduced from the slice dose profile measurements using normalised organ dose data and may in turn be used to compare the radiation consequences of these three-dimensional images with standard cross-sectional images.

## THE RADIOLOGICAL RISKS FROM X-RAY EXAMINATIONS AND NUCLEAR MEDICINE PROCEDURES

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*National Radiological Protection Board, Chilton, Didcot, Oxon*

Recent national surveys conducted by the NRPB have provided a reliable indication of the average doses received by patients from routine X-ray and nuclear medicine examinations. Information on the distribution of patient ages and sex for these examinations was also collected during these surveys. Taken together, these data have enabled us to estimate the probable radiological risks associated with routine diagnostic procedures Four types of detriment have been considered· fatal and non-fatal cancers, genetic effects and effects on the fetus For the somatic effects, the often long delay between exposure and appearance of radiogenic cancers and its relation to the natural life-expectancy of typical patients has been taken into account. Similarly the child-expectancy of typical patients has been allowed for in estimating the probability of genetic effects occurring. Recent information suggesting an enhanced sensitivity of the fetus to radiation between the eighth and 15th week of gestation has been included in the assessment of the risks of fetal exposure. Results are presented which illustrate the approximate probabilities of these adverse health effects occurring for the average patient exposed to a number of routine X-ray and nuclear medicine examinations

## A STABLE BEAM CALIBRATION SYSTEM

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Dosemeters used for the specification and monitoring of the output of the various treatment modalities used in radiotherapy have been subject to regular calibration for many years and a system has evolved in the UK of secondary standard dosemeters being presented for calibration at the National Physical Laboratory. In recent years, there has been increasing awareness of the need to calibrate protection-level dosemeters and this has led to a requirement for the calibration of these dosemeters being included in Regulation 24 of the Ionising Radiations Regulations 1985, while Paragraph 154 of the Approved Code of Practice states that all instruments should be individually calibrated before use.

While the number of dosemeters in use in departments of radiotherapy for treatment purposes is limited, the numbers of dosemeters used for the various facets of radiation protection are much greater and to follow the calibration procedures currently in use for therapy-level dosemeters would be expensive and time consuming. A calibration system has therefore been developed, based on a stable radiation beam, the characteristics of which are accurately known and specified Various radionuclide sources are used to provide a range of photon energies and the system provides a wide range of dose rates, suitable for many applications. The beam itself is capable of calibration to the accuracy of a primary standard, so that intercomparison with another standard dosemeter is unnecessary, while suitable dosemeters can be ascribed secondary standard status. Two dosemeters may be calibrated in the same series of measurements, which can be programmed and carried out entirely automatically under microcomputer control in a period of a few minutes, and a printed record of the calibration produced, which can be issued as a calibration certificate

## QUALITY ASSURANCE PROCEDURES IN EXTERNAL-BEAM RADIOTHERAPY AT THE LONDON HOSPITAL

R. A. Lake, A. K. Morgan and S. C. Klevenhagen

*Department of Medical Physics, The London Hospital*

Routine quality assurance of radiotherapy treatment machines is essential for accurate treatment of malignant disease In a large department, such quality assurance is both time consuming and labour intensive, especially for linear accelerators We have designed and made equipment which minimises the time spent making these routine measurements Sealed ionisation chambers are used daily by the radiographers for output measurements on all X-ray machines. They are calibrated weekly against an output measured with a Farmer dosemeter in a water-substitute phantom made from epoxy-resin-based materials. Other phantoms have been made which facilitate the rapid checking of electron and photon energies following servicing and maintenance of linear accelerators Symmetry plots for both photon and electron beams are produced by driving a chamber within a solid phantom across the field of radiation. This poster describes the quality assurance equipment and explains the procedures for its use Sample results of some of the check procedures are presented

## CONTAMINATION MONITORING OF THE PUBLIC FOLLOWING CHERNOBYL

P. P Dendy, *R. Massoumi, †K. E. Palmer and *K. F. Szaz

*Department of Medical Physics, *Department of Nuclear Medicine and †East Anglian Regional Radiation Protection Service, Addenbrooke's Hospital, Hills Road, Cambridge*

Following the accident at Chernobyl, many members of the general public required reassurance that levels of radioactivity both within their body and on their person did not constitute a significant hazard Early measurements were on people returning from Eastern Europe and Scandinavia and some 50 persons in this category were monitored in the whole-body counter at Addenbrooke's Hospital. Several radionuclides were present but an estimate of activity was made only for $^{131}$I, primarily because of the poor energy resolution of the sodium iodide detectors The results are presented Subsequently, 39 persons from the Cambridge locality were monitored and $^{131}$I levels estimated. Levels in children were not significantly different from those in adults. In the months following Chernobyl caesium levels have been monitored Initial measurements were made about 3 months following the accident Repeat measurements after a further 3 months showed the levels had, on average, approximately doubled. Results are presented and compared with those measured in persons, on the same equipment, in the early 1960s following cessation of atmospheric testing of nuclear weapons. Neither the initial iodine level nor subsequent caesium levels measured in the local inhabitants are sufficient to cause alarm or necessitate any action However, monitoring has proved extremely valuable and is the only satisfactory way to reassure the public In order to provide rapid local reassurance and to identify persons who may require more rigorous dose assessment, such as could be provided by whole-body monitoring, regional emergency plans for future nuclear incidents of this type propose the setting up of about 20 local monitoring stations throughout the region. These stations would utilise monitors in day-to-day hospital use and would be staffed by personnel familiar with the monitor in their routine work. The stations could be sited in local health centres and would thus provide immediate information for general practitioners A map showing the proposed distribution of these monitoring stations is given.

### CHANGES IN THE PATTERN OF REFERRALS TO THE RADIOLOGY DEPARTMENT BY CLINICAL SPECIALTY

F. A. Paris and *W. Hull

*Radiology Department, Northwick Park Hospital, Harrow, Middlesex and *Centre for Health Planning and Management, University of Keele*

Information was collected during three 1-month sample periods to determine the workload referred to the radiology department by each clinical specialty These sample periods were 2 years apart. For each period the change in consultant staffing of each clinical specialty was investigated. This poster demonstrates the workload for selected clinical specialties and the influence of changes in consultant staffing on the referral pattern and imaging modality requested for each sample period There is a need for a radiology department to be able to anticipate changes in referral pattern which will affect the departmental budget.

### WORKLOAD IN AN DEPARTMENT OF DIAGNOSTIC IMAGING

F. A. Paris and *W. Hull

*Radiology Department, Northwick Park Hospital, Harrow, Middlesex and *Centre for Health Planning and Management, University of Keele*

Information concerning the workload through the radiology department was collected on a computer over a 14-month period. For selected clinical specialties and individual clinicians, the results are presented by: patient attendance, workload units, and Korner units Attention is drawn to the need for a comprehensive and accurate method of data collection if good management of resources in the radiology department is to be practised The poster compares the collection of Korner data using various weighting factors and raises the question as to whether statistics as presently (or as about to be) collected can become satisfactory performance indicators for the activities of a radiology department

### TELERADIOLOGY. IMAGE TRANSMISSION VIA THE STANDARD TELEPHONE NETWORKS, WITH IMAGE STORAGE AND RECOVERY SYSTEMS

R. Atkinson and *C. Redman

*X-ray Department, Norfolk and Norwich Hospital, Norwich and *Compact Imaging Ltd, London*

The receiving station and equipment are described, and the method and experience of operation as a routine recall system illustrated. The anticipated advantages which influenced the decision, the cost and actual known or perceived results are discussed. The transmitting station network and equipment are described, together with the current and future world-wide operation of this advanced telecommunications system The simplicity, low cost, present and future advantages over present practice (unchanged for the past 50 years) are discussed.

## Posters. Radiotherapy

**Chairman: Dr R. D. James**

Iridium-192 brachytherapy in the treatment of prostatic cancer, by A T. Porter, J. E. Pedersen, A M Aref and J. S. Pocha
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### IRIDIUM-192 BRACHYTHERAPY IN THE TREATMENT OF PROSTATIC CANCER

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Fifty patients with clinical stage B2 and C adenocarcinoma of the prostate have been treated with a combination of afterloaded iridium brachytherapy and external-beam radiation therapy. After clinical staging, including a bone scan and acid-phosphatase level estimation, a staging lymphadenectomy is performed. At the same time the prostate is implanted transperineally, with between 15 and 18 guide needles, using a template. These guide needles are subsequently loaded with ribbons containing iridium-192 seeds A dose of 3500 cGy is prescribed to an isodose curve encompassing the prostate gland at a dose rate of 60–75 cGy $h^{-1}$ Following the implant, a further 4500 cGy external-beam radiotherapy is delivered to the pelvis or prostate, depending on the nodal status The fifty patients have now been followed for a mean duration of 13 (range 2–50) months Twenty-two patients have undergone transperineal prostatic biopsies at 12 months. Eighteen of these are negative. The mean hospitalisation period for implant is 7 (range 6–11) days Only three serious complications related to this treatment have been recorded to date: one rectal wall ulceration and two abdominal wound infections. A detailed description of the technique, its early results and complications are presented

### TWELVE-YEAR SURVEY OF WILMS' TUMOURS

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Sixty-six cases of Wilms' tumours were followed up for over 12 years from 1974. There were 36 males and 30 females. The majority were 1–5 years old. Two children had the bone metastasising type of Wilms' tumour. The associated abnormalities were hemihypertrophy, two cases, multiple exostosis, two cases, and Beckwith-Wiedemann syndrome, one case. Only two tumours were confined to the capsule at presentation. Others broke into the renal parenchyma and often caused loss of function Three (5%) were bilateral and three (5%) showed calcification One tumour was extrarenal, lying attached to the underside of the left ureter. Secondary spread was skeletal in one, fatal case, hepatic in one, again fatal case, and pulmonary in 13 cases, three of which proved fatal Other chest complications included 16 cases (25%) of single or recurrent attacks of pneumonia. None was caused by opportunistic invaders. Pleural effusion was seen in three cases, all associated with metastases. Pulmonary embolism and infarction due to tumour embolus occurred during nephrectomy in one girl She recovered later. Post-operative pneumothorax developed in two cases. One boy had hypertension and cardiomegaly resulting from renal failure Except for metastases, none of the chest complications were fatal. Thirty-four patients (50%) had normal chest radiographs throughout Prognosis is good and shows further improvement over the last decade. Fifty-five patients (80%) are alive and well, six were lost for follow-up, and five (7.5%) died, all of whom had secondaries.

# *Proceedings of The British Institute of Radiology*

## TRANSITION ZONE DOSIMETRY IN RADIOTHERAPY

M. G. Samarasekara and F. R. Hudson

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The dose distributions in the vicinity of exposed dental amalgam have been measured for 5 MV and for $^{60}$Co beams, using film and ionisation chamber techniques. Data on the dose distribution inside the amalgam were deduced from measurements made using lead foils. An analysis of the dose distribution is presented in terms of the secondary charged particles produced in adjacent high- and low-atomic-number materials Techniques to minimise unfavourable transition-zone effects and to enhance favourable effects in radiotherapy treatment are discussed. An example is considered in which transition-zone effects could be employed to enhance the tumour dose achieved in the treatment of carcinoma of the oesophagus by the use of backscatter effects derived from barium sulphate. The possible use of intraoral high-density material for dose enhancement is also discussed

## PULMONARY CHANGES IN BREAST CANCER PATIENTS TREATED BY THREE DIFFERENT RADIOTHERAPY TECHNIQUES

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Computed tomography (CT), ventilation perfusion scanning (VQ) and single-photon emission computed tomography (SPECT) were used to assess the pulmonary complications following radiotherapy for carcinoma of the breast. Three radiotherapy techniques were used. The first group (four fields), following mastectomy, had an anterior field to treat the internal mammary, axillary and supraclavicular nodes, a posterior field to the axilla and an opposed pair of fields to treat the chest wall. The second group (three fields), following lumpectomy for medially placed tumours, had an opposed pair of fields to treat the breast and axilla with a third anterior field to treat the internal mammary nodes The third group (two fields), following lumpectomy, were treated with an opposed pair to include the breast and axilla

Computed tomography and SPECT were more sensitive at detecting abnormalities than VQ scans The CT scans from patients treated using the four-field technique commonly showed opacification at the apex and in the anterior mediastinum, with loss of pulmonary vascular markings; SPECT showed absent or impaired perfusion in these areas, including non-irradiated lung Those patients treated using the three-field technique had opacification in the anterior mediastinum and subpleural area of the anterior chest wall on CT; SPECT demonstrated absent or decreased perfusion in these areas and in some patients quite extensive perfusion defects in the lung distant from the radiation fields There were fewer abnormalities in patients treated by the two-field technique. The CT scans showed opacification in the subpleural area of the anterior chest wall and corresponding perfusion defects were demonstrated by SPECT We conclude that CT and SPECT can show pulmonary damage in patients receiving radiotherapy for breast cancer. These changes are most extensive in patients who have had irradiation of the anterior mediastinum and SPECT suggests that treatment of the hilar vasculature may cause extensive perfusion defects in both lungs. Because of these findings and the knowledge that treatment of the internal mammary nodes does not improve survival, we no longer treat the anterior mediastinum following mastectomy or lumpectomy for medial tumours.

## SPLIT-COURSE RADIOTHERAPY IN COMBINATION WITH CIS-PLATINUM IN PATIENTS WITH ADVANCED CANCER OF THE CERVIX

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Ten patients with locally advanced poor prognosis squamous cancer of the cervix have been treated by a combination of radiotherapy and cis-platinum at the time of writing. External-beam radiotherapy is given using a 6 or 15 MV linear accelerator by a four field "box technique" A tumour given dose of 5000 cGy is delivered in 20 equal fractions over 42 days treatment being given on week days between days 1–14 and 29–42 Cis-platinum 50 mg/m$^2$ is given by intravenous infusion on days 1, 14, 29 and 42, (1½–2) hours before radiotherapy

Patients are assessed before treatment with history, examination, complete blood count, SMA 12, chest X-ray, isotope renogram, CT scan, lymphangiography, cystoscopy, sigmoidoscopy and examination under anaesthetic. After treatment has been completed as described above a further assessment with evaluation under anaesthetic is carried out and treatment continued on an individualised basis depending on response to treatment. Ideally, intracavitary radiotherapy is given on a Selectron giving a dose of 3000 cGy to point A, at a dose rate of 60–70 cGy per hour.

Throughout treatment and follow-up morbidity is carefully assessed and has been recorded accordingly to the Gynaecological Oncology Group adverse effects criteria. No acute morbidity with a score greater than 2 has been seen.

Response to treatment has been very encouraging and results will be presented. On the basis of this pilot study, a randomised study has been proposed to investigate whether the addition of cis-platinum to split-course radiotherapy for locally advanced squamous cancer of the cervix will improve local control and delay systemic relapse without increasing the morbidity of treatment.

## THE TONGUE AND FLOOR OF MOUTH AS DEMONSTRATED ON COMPUTED TOMOGRAPHY

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Computed tomography (CT) is important in staging patients with carcinoma since the degree of tumour involvement determines the modality and extent of treatment In head and neck oncology, CT has been shown to be of great value in determining the spread of tumours within the laryngeal framework by identifying invasion of tissue planes and involvement of important structures. We suggest that CT is also of considerable value in staging of patients with carcinoma of the tongue and floor of mouth. Because the anatomy of the floor of mouth is complex, difficulties in interpretation can be overcome by familiarity with normal structures. For accurate assessment of the normal musculature, contrast-enhanced, narrow CT sections both in the axial and coronal plane are necessary. We illustrate the normal anatomy of this region with CT sections and accompanying line drawings.

## PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: EXPERIENCE AT ADDENBROOKE'S HOSPITAL, CAMBRIDGE

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A series of 22 cases of this rare tumour is reported. Two cases were associated with rheumatoid arthritis, but none of the others showed any evidence of immunosuppression. The mode of presentation and natural history were similar to adult high-grade glioma but, despite better radiation responsiveness, the mean survival was only 18 months. The male: female ratio was 2 14·1, the mean age at presentation was 63 (range 47–72) years Single tumour masses were present in 77% (17 out of 22) and the frontal lobe was the commonest site (14 out of 22, 64%) After treatment with varying degrees of surgical excision and cranial irradiation, 17 of the 22 patients are dead, 12 because of persistent or recurrent intracerebral disease (two died of other causes and in three the cause of death was uncertain) Five patients are still alive at 51, 12, 10, 9 and 6 months, respectively Failure to eradicate intracranial tumour was the main reason for failure to cure these patients, and no case presented with clinical evidence of spinal disease, or relapsed there. Spinal treatment should be reserved for those cases where the cerebrospinal fluid cytology is positive and the primary tumour is controlled. Correlation of histology, computed tomography and angiographic findings indicate that these tumours do not readily form their own neovasculature, but tend to grow in a parasitic fashion along existing blood vessels and are extra-axial The possible future role of hyperfractionation and chemotherapy are discussed in the light of the above findings.

## TESTICULAR TUMOUR MARKERS. COMPARISON OF VALUES FROM PERIPHERAL BLOOD WITH SPERMATIC-VEIN BLOOD

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The markers for testicular cancer, alpha-fetoprotein and human chorionic gonadotrophin, have been measured both in peripheral blood and in spermatic-vein blood taken at the time of orchidectomy These studies show that the concentration of marker(s) in spermatic-vein blood is often higher than in peripheral blood It is assumed that this difference in concentration exists because the spermatic vein drains directly from the tumour and its contents have not yet been diluted. Such measurements are of particular value in patients whose tumours produce only small amounts of marker(s) such that, although detectable in spermatic-vein blood, the concentration is below the level of detection in peripheral blood In patients who already have metastatic disease at the time of orchidectomy, very much less difference is often observed between marker concentration in spermatic-vein blood and that in peripheral blood. This may be attributed to the production of marker(s) by the metastatic deposits as well as by the primary tumour. Examples illustrating these findings are presented and discussed (These studies have been carried out in collaboration with the South West Testicular Tumour Study Group and the South West surgeons.)

## COPPER AND ZINC REFLEXES IN RADIOTHERAPY

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The inverse relationship of protein-bound copper and zinc is known to occur in a wide variety of pathological states, and high-dose zinc supplements have recently been found effective in the management of hepato-lenticular degeneration (Wilson's disease). In this paper recent evidence from zinc mobilisation studies after surgical trauma are compared with previous studies in radiotherapy with megavoltage irradiation In both, the results indicate a very rapid initial elevation of plasma zinc levels followed by a reflex fall as the zinc is taken up for protein synthesis, and this is accompanied by zinc losses in urine The specific role of copper-related enzymes in tumour collagen formation is demonstrated in experimental copper depletion induced by prolonged zinc supplements in C3H mice bearing mammary adenocarcinoma The histology of the copper-depleted mice shows tumours with marked reduction in stroma and increased invasion of blood supply compared with controls and suggests that the classic features of Hodgkin's-type lymphomas are dependent on the relative activity of zinc- or copper-related metalloenzymes The seemingly instantaneous elevation of plasma zinc after surgical incision suggests a neuro-hormonal response which, coupled with zincuria, highlights one of the mechanisms whereby pain can debilitate.

## ALTERATION OF RADIATION SENSITIVITY IN MAMMALIAN CELLS TREATED UNDER HYPOTONIC CONDITIONS *IN VITRO*

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The influence of hypotonic treatment on the survival of irradiated Chinese hamster ovary (CHO) cells was studied by us at the University of Texas at Galveston. Hypotonic media were produced by a serial dilution of Hsu's medium (273 mosm/kg) without serum with distilled water In all instances, unirradiated cells were used as a control (with and without hypotonic treatment) and untreated, irradiated cells were carried through all the same procedure steps as those with hypotonic treatment Contrary to our expectation, hypotonic treatment produced radiosensitisation in the investigated mitotic and asynchronous cells The survival curves of both mitotic and asynchronous cells are of exponential, low-threshold type. Ultrastructural study of mitotic and interphase cells indicated that "heterochromatin" could be reversibly decondensed by hypotonic treatment Metaphase chromosomes were greatly extended and chromatin fibres reduced from 250–400 Å to finer filaments of 70–160 Å in diameter. Chromatin of interphase nuclei was decondensed and the chromatin filaments could be seen extending from the nuclear envelope into the surrounding nucleoplasm. The nucleolus was reversibly dispersed by the hypotonic treatment These studies suggest that the increased radiation damage induced by hypotonic treatment is due to "uncoiling" of deoxynucleoprotein. The effect of anisotonic treatments on cellular radiosensitivity and ultrastructure as reported by others is briefly reviewed It appears that the toxicity of hypotonic solutions in the osmolalities which would be advantageous therapeutically precludes other than limited local use. More promising would be the use of certain drugs which induce cellular swelling at iso-osmotic conditions. Malignant cells might be more sensitive to the non-toxic plasma levels of these drugs (*e.g* ethacrynic acid) which may, at the same time, act as efficient radiomimetic agents

## THE CHOICE OF MATERIALS FOR IMMOBILISATION SHELLS

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An increasing number of materials has become available for use in the preparation of immobilisation shells for radiotherapy. The advantages and disadvantages of using the more traditional vacuum-formed shells are contrasted with those met with in the new, lower-temperature thermoplastics. The clinical suitability and physical parameters of commonly used materials are reviewed and estimates of the cost, in materials and time, of preparing shells from them are presented Examples of shells prepared from a variety of materials are shown. The properties of the ideal shell-preparation material are proposed.

## VOCAL QUALITY 10 YEARS AFTER RADIOTHERAPY FOR EARLY GLOTTIC CANCER

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In treating laryngeal cancer, the aims of radiotherapy are to cure the disease and to preserve the voice, and its ability to achieve both of these is undisputed, but the long-term quality of the preserved voice has not previously been documented. We were able to trace and perform formal vocal assessment on 12 patients (11 male) who had undergone radical radiotherapy for Stage I squamous carcinoma of the vocal cord at least 10 years previously Vocal quality was assessed, as well as by a number of more refined techniques, on a subjective five-point scale (0 = no voice, 1 = severe impairment, 2 = moderate impairment, 3 = slight impairment, 4 = normal) Assessments were made by the patients themselves, by an independent untrained observer, and by a speech therapist. The number of patients accorded each score by the various observers is given in Table I

TABLE I

| | Score | | | | |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Patient | 0 | 0 | 5 | 3 | 4 |
| Independent observer | 0 | 0 | 3 | 7 | 2 |
| Speech therapist | 0 | 6 | 4 | 2 | 0 |

This shows that, while patients regarded their voices as normal to moderately impaired, there are, objectively, quite significant abnormalities. As acceptability to patients is the more important criterion, these findings confirm the satisfactory results of treatment

## HISTOLOGICAL CHANGES FOLLOWING INTERSTITIAL HEATING OF RAT SPONTANEOUS MAMMARY CARCINOMA

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In order to assess the value of a 27 MHz interstitial hyperthermia system, a comparison between the histological appearances of heated and unheated rat mammary carcinoma has been made. The transplanted rat mammary carcinoma, originally of spontaneous origin, was initiated by subcutaneous implant and grown for 14 days before treatment. Animals, with tumours of maximum diameter 1–1.5 cm, were then matched for size with controls and treated with the interstitial hyperthermia unit to produce a maximum temperature within the lesion of 49°C, which was maintained for 25 min. Histological analysis was performed on the tumours of these animals, sacrificed between 1 day and 10 days after treatment, and compared with controls. There was a significant increase in the percentage area of tumour necrosis in the heated animals compared with controls which was maximal at 10 days after treatment. There was also a significant decrease in the mitotic activity of the heated tumours compared with controls.

## THE *IN-VIVO* STAGING OF RECTAL TUMOURS. AN ASSESSMENT OF CURRENTLY USED TECHNIQUES

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Fifty-two patients with rectal neoplasms (46 malignant and six benign) have had a pre-operative digital examination, rectal endosonography (ES) and computed tomography (CT). In all the benign tumours digital examination and ES correctly predicted containment within the mucosa/submucosa while CT could only show confinement to the rectal wall. Pre-operative assessment of the rectal cancers showed that digital examination had an accuracy of 69% and predicted invasion beyond the muscularis propria with a sensitivity of 73%, specificity of 83%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 43%. Computed tomography similarly had an accuracy of 80%, sensitivity of 84%, specificity of 63%, PPV of 91% and NPV of 45%. Endosonography was, overall, the most accurate method of assessment of local invasion and when compared with post-operative histopathology had a correlation coefficient of 0 85 ($p < 0\,001$) (Rank Spearman). Its accuracy was 91%, sensitivity 95%, specificity 87%, PPV 96% and NPV 78%. Endosonography is a more accurate and objective method for staging rectal cancer than other commonly used techniques, in particular digital examination and CT.

## THE *IN-VIVO* ASSESSMENT OF LYMPHATIC METASTASES IN RECTAL CANCER

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Rectal endosonography (ES) is an effective method of assessing local invasion in rectal tumours, but is it possible to identify involved pararectal lymph nodes using the same technique? We have examined 93 patients with primary rectal cancers using a Bruel and Kjaer 1846 scanner in conjunction with a rotating endoprobe and 5.5 MHz and 7.0 MHz transducers. Eighty-six of these patients subsequently underwent resection of their tumours, which were subjected to detailed histological examination. Lymph nodes were predicted to be involved in 44 cases by appearance and size. Comparison of the endosonographic prediction of involvement with the histopathological findings gave an overall accuracy of 78% and correlation coefficient of 0.58 ($p < 0.001$) The sensitivity of the investigation was 85%, specificity 73%, positive predictive value 75% and negative predictive value 83% There was no correlation of false positive diagnoses with any histological architectural feature. Endosonography is a more accurate method than any other currently available for the detection of lymphatic metastases in rectal cancer

## SURVIVAL OF PATIENTS PRESENTING WITH BREAST CANCER IN THE WEST MIDLANDS IN THE YEARS 1960 AND 1975

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We have attempted to identify any changes in the prognosis in the general population of women with breast cancer by examining the survival of all patients first diagnosed in the West Midlands region during the years 1960 (1452 women) and 1975 (1862 women), by when most of the therapies in current use had been introduced Data on age at diagnosis, stage primary treatment, relapse data and date of death were collected from the records of the West Midlands cancer registry. Overall there was an improvement in survival for patients diagnosed in 1975 ($p = 0.0007$, median survival for 1960 = 55 months, for 1975 = 72 months). When divided into early (Stage I and II) and late (Stage III and IV) tumours this survival advantage was found to be confined to the early stages (median survival 115 months for 1960 patients but over 10 years for 1975 patients) although there was a trend towards improved survival stage by stage Disease-free survival was improved for 1975 patients ($p = 0.0014$) with most of the divergence occurring within the first 2 years after diagnosis Survival after relapse was also better for 1975 patients ($p = 0.03$) but the differences occurred mainly between 12 months and 48 months after relapse, with a similar, but not statistically significant ($p = 0.08$) picture for patients who presented with metastatic disease This improvement for patients with disseminated disease occurred after the median survival was reached and so this was not affected, with the largest differences being evident at the 25th centile. In summary, the prognosis in 1975 was better than in 1960, partly because of an improvement in disease-free survival (probably due to earlier presentation, although an effect of treatment cannot be excluded) but also because the treatment of disseminated disease was more effective in 1975 than in 1960.

## DOSIMETRY OF LUMBAR AND INTRAVENTRICULAR CEREBROSPINAL FLUID ADMINISTRATION OF IODINE-131 MONOCLONAL ANTIBODIES

R. B. Richardson, A. G. Davies, G. E Staddon, R. P. Moseley, J. T. Kemshead, P. C Jackson and H. B. Coakham

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Radioiodinated monoclonal antibodies (MCAs) have been administered to seven patients with disseminated tumour in the cerebrospinal fluid (CSF) space. Specific binding to tumour has been shown Therapeutic doses of $^{131}$I labelled to appropriate MCAs have resulted in clinical remission and prolonged survival Dosimetry calculations assuming thin-layer tumour have been carried out, giving insight into the constraints of the model and its clinical relevance. The clearance of activity from the spine and head were obtained by external probe or gamma camera. The slow component of the biexponential clearance can be shown to represent tumour-specific binding. Three patients received $^{131}$I tumour-specific MCAs (890–1590 MBq, 24–43 mCi) which resulted in a mean absorbed dose of 7 and 6 mGy/MBq (26 and 23 rad/mCi) to the thoraco-lumbar region of the spine and the subarachnoid space of the head respectively, when assuming diffuse distribution in the CSF alone When a binding factor is taken into consideration, there is an increased absorbed dose of 46 mGy/MBq (167 rad/mCi) to tumour of the spine, while there is little change in the absorbed dose to the head Supportive evidence of specific uptake of $^{131}$I-labelled MCA by tumour sites was seen in the scintigrams Intraventricular administration has been adopted in recent cases, in preference to lumbar administration, to obtain better distribution of radiolabelled MCA throughout the CSF pathways.

## ASSESSMENT OF THE COMPUTER-CONTROLLED PHILIPS SL25 ACCELERATOR FOR CONFORMATION THERAPY

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The Phillips SL25 accelerator recently commissioned at the Royal Marsden Huspital, Surrey, incorporates complete micro-processor control There is full software control of gantry and collimator-head rotation, as well as the motions of the four collimator jaws and wedge before and during treatment. The SL25 accelerator is thus capable of conformation therapy without special modification. A preliminary evaluation of the SL25 with respect to reproducibility of set-up, dynamic control of movements and the suitability of the software provided has been made and the results are presented In particular, the matching of adjacent static fields produced by software-controlled asymmetrical collimator motion and mechanical response times have been investigated.

## NON-LINEAR EFFECTS WITH FOCUSED ULTRASOUND IN TISSUES: AN APPLICATION FOR HYPERTHERMIA

W. Swindell

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Previous work (Swindell, 1985) has predicted that non-linear effects associated with focused ultrasound in tissue will result in an elevation of absorbed-power density near the focus relative to that expected without non-linear propagation This is caused by the increased absorption of higher harmonics (produced by the conversion of acoustic energy from the fundamental frequency into the higher modes) and by the losses associated with the passage of an acoustic shock wave which may be present if the non-linear interactions are strong enough. Swindell (1985) pointed out that the model should, and could, be improved in at least two ways: the diffraction phase propagation terms of the fundamental and higher harmonics should be considered, and the focusing properties of each harmonic should be considered separately. This work describes some of the results that are obtained when these improvements are incorporated in the model Even greater enhancements are then predicted in the region of focus. Also, the predicted pressure waveforms in the region of the focus more closely match those expected on the grounds of diffraction theory and those which are actually observed in practice. The application of this work is in the use of ultrasound for delivering thermal energy to tissue at depth with a high degree of spatial selectivity.

## REFERENCE

SWINDELL, W , 1985 A theoretical study of non-linear effects with focused ultrasound in tissues: an "acoustic Bragg-peak". *Ultrasound in Medicine and Biology, 11*, 121–130.

# 1987 Mayneord Lecture (sponsored by 3M UK PLC)

## CHERNOBYL REACTOR ACCIDENT: THE IMPACT ON THE UNITED KINGDOM

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The accident at the Chernobyl nuclear power station in the western Ukraine on April 26, 1986, led to widespread contamination and confusion in both Europe and the rest of the world This paper considers the response in the UK, the radiological impact of the accident and the lessons for the future.

The arrangements for environmental monitoring and for dealing with emergencies, as they existed at that time, are reviewed The actual sequence of events in the early aftermath of the accident is then described. Measurements were made of external dose, concentrations in air and in deposition. Activity in milk, vegetables, meat and human beings was monitored. Results of all measurements were co-ordinated, preliminary estimates of doses were made and advice was formulated. All of these functions had been expected for the circumstance and were well prepared for. Some of the other demands on resources—such as monitoring vehicles and travellers, monitoring abroad and the vast number of enquiries from public, parliamentarians and press—were not expected. In the longer term, the high deposition in some areas led to restrictions on the movement and slaughter of sheep and lambs and required extended monitoring programmes. International trade was hindered by import restrictions and this led to a long-term requirement for the monitoring of foodstuffs.

The scientific interest of such an event was not neglected. The transfer of radionuclides through foodchains to man has been followed. Investigations have continued throughout the winter to permit confident predictions of future levels. These studies are described, the results are presented and the implications for future monitoring programmes are drawn. The radiological impact on the UK is determined by an evaluation of the collective dose to the population and the calculation of potential health effects Finally, some consideration is given to the lessons learnt, the impact of this accident on future emergency plans, the use that should be made of expertise in organisations other than the nuclear industry, the requirement for radiological consistency internationally and the need to maintain public confidence by good communications.

# Therapeutic Ultrasound. One-Day Seminar

**Chairman: Professor P. N. T. Wells**

Turning the power back up: introduction and overview, by C. R. Hill
Biophysics and thermal biology, by G ter Haar
Experimental basis of physiotherapy, by M. Dyson

## TURNING THE POWER BACK UP: INTRODUCTION AND OVERVIEW

C. R. Hill

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It is now just 70 years since it was first recognised that ultrasound, as a directional, penetrating and energetic form of radiation, might have important potential for the treatment of disease. The subsequent history of the investigation and practical application of the underlying phenomenon provides some good illustrations for Koestler's "Sleepwalkers" model for the progress of science.

Practical techniques for the therapeutic use of ultrasound fall into two broad categories, in which treatment entails *either* a highly localised exposure that can be actually or potentially totally destructive to tissue within a selected region, *or* a relatively widespread exposure that is generally not inherently destructive to tissue. The various papers in this symposium illustrate these two approaches. The latter has considerable similarities to techniques using radiofrequency and microwave radiations and has found widespread, if somewhat empirical, use in physical medicine. The outstanding feature of ultrasound, however, is its ability to localise energy deposition, either remotely through beam focusing or by vibration of the tip of a surgical tool, and it is undoubtedly in this area that there is major unexplored potential, not least for local control of cancer

### BIOPHYSICS AND THERMAL BIOLOGY

Gail ter Haar

*Physics Department, Institute of Cancer Research, The Royal Marsden Hospital, Sutton, Surrey*

Ultrasound is used therapeutically at a range of different acoustic intensities. Where beneficial, non-lethal, biological changes are sought (for example, in physiotherapy), intermediate levels (0.125–3.0 W cm$^{-2}$) are used. Surgical applications and hyperthermia techniques aim at cell killing and, therefore, exposure levels are higher. The way in which ultrasound interacts with tissue to produce biological change is only partially understood. A number of different mechanisms can be highlighted. The absorption of ultrasonic energy leads to a temperature rise. This may or may not be biologically significant, depending on the ultrasonic intensity and the type of tissue being irradiated. The other major mechanism that may operate in tissue is acoustic cavitation. This is a proven mechanism for change *in vitro*, and there is now good evidence that it can occur in intact tissues *in vivo*. Other non-thermal interaction mechanisms are postulated, but it is more difficult to prove that these occur *in vivo*. Each interaction mechanism has an intensity threshold at which it becomes biologically significant. As the intensity is raised, more mechanisms come into play until, at sufficiently high levels, no one mechanism dominates.

### EXPERIMENTAL BASIS OF PHYSIOTHERAPY

Mary Dyson

*Division of Anatomy, UMDS (Guy's Hospital Campus), London*

Ultrasonic therapy is widely used by physiotherapists to accelerate tissue repair and to reduce pain. Experimental evidence that it can affect the inflammatory, proliferative and remodelling phases of tissue repair is described. Recent indications that a placebo effect can be involved in pain relief and possibly also in the reduction of inflammation *in vivo* are examined. The results of *in-vivo* and *in-vitro* investigations into the biological and biophysical mechanisms involved in the stimulation of repair processes by ultrasound are described, topics introduced include changes in membrane permeability, thermal effects, cavitation and microstreaming.

## Session II

**Chairman: Dr P. Davies**

Ultrasonic surgical vibrators/aspirators, by D. J. Watmough
Ultrasonic treatment of Menière's disease, by M. Halliwell
Local ultrasound hyperthermia, by K. Hynynen
Lithotripsy, by D. Rickards

### ULTRASONIC SURGICAL VIBRATORS/ASPIRATORS

D. J. Watmough

*Department of Biomedical Physics and Bioengineering, University of Aberdeen and Grampian Health Board*

Magnetostrictively driven vibrating probes, such as the Cavitron, are now used in surgery for removal of certain brain tumours and for hepatic and renal surgery. Not only are the capital costs of the device high but so are the running costs because the vibrating tips have to be changed after each operation. Our group has established a straightforward method of measuring their efficiency at tissue removal. The mode of action of the device has also been investigated, though further work in this direction is still needed. Whereas the Cavitron is a resonant device operating at a single frequency of 23 kHz, we have built a sonic version whose frequency and amplitude can be varied. This new device has enabled us to measure tissue removal rate as a function of frequency and displacement amplitude. Surprisingly, above 300 Hz the removal rate does not appear to increase further. We have also varied tube diameter and been able by this simple expedient to almost double the tissue removal rate. The shape of the tip is also found to be significant in determining these rates.

The main virtue of the device is that the tip emulsifies soft tissues but blood vessels, which are elastic, are not damaged, indeed are left intact. Bearing in mind the time at operation is affected by removal rates, any increase may be significant in reducing risk and also in economic terms.

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CHAN, K. K., WATMOUGH, D. J., HOPE, D. T. & MOIR, K., 1986. A new motor driven surgical probe and its *in vitro* comparison with the Cavitron ultrasonic surgical aspirator. *Ultrasound in Medicine and Biology, 12*, 279–283.

### ULTRASONIC TREATMENT OF MENIÈRE'S DISEASE

M. Halliwell

*Department of Medical Physics, Bristol General Hospital*

Menière's disease is a disorder of the inner ear which is characterised by recurrent attacks of vertigo. Treatments include diet, drugs and surgical ablation of the inner-ear function. Ultrasonic surgery offers the possibility of the destruction of vestibular function, and hence suppression of the symptoms, while maintaining the function of the cochlea, thus leaving hearing intact.

The first use of ultrasound for this condition was described by Krejci in 1952 and it was developed further by Arslan in 1953. Initial results were sufficiently promising to warrant considerable development to be undertaken, improving the physical construction of the applicator and the reliability of the generator. A commercial device became available in the United Kingdom in 1964. However, the technique required considerable skill and technical back-up, consequently only a few centres developed sufficient expertise to make the procedure a routine treatment. Although the current operative details vary considerably from centre to centre, several modifications have been made to both applicator and generator design, leading to a straightforward technique requiring very little in the way of technical back-up at the time of operation

### LOCAL ULTRASOUND HYPERTHERMIA

Kullervo Hynynen

*Department of Radiation Oncology, University of Arizona Health Sciences Center, Tucson, Arizona, USA*

During the past 10 years, local hyperthermia combined with radiotherapy has been shown to have a great potential in the treatment of superficial tumours However, it has been difficult to extend the same response to tumours deep in the body because of the technical difficulties of heating them The most promising method to heat deep-seated tumours is focused ultrasound. In this paper the physical factors affecting the temperature distribution induced during scanned, focused ultrasound hyperthermia are discussed Finally, a patient treatment system is described and experiences from the first patient treatments are evaluated.

### LITHOTRIPSY

David Rickards

*Department of Radiology, Middlesex Hospital, London*

Endoscopic and extracorporeal techniques have now advanced to a stage where they have virtually displaced open surgical methods as a first line of management of urinary tract calculi of almost any size and at any site. Development continues and these techniques are becoming more affordable (though still very expensive), more effective and easier to perform. Percutaneous renal access to the kidney and the subsequent extraction of stones in one piece is limited by the size of tract made. The development of stone fragmentation produced both ultrasonic and electro-hydraulic lithotripsy, both used in conjunction with a percutaneous approach to the kidney. Electro-hydraulic probes act by a microsecond electrical discharge under water, causing a spark which in turn sets up a shock wave, fragmenting the stone which can then be removed in pieces The action of the shock wave is to cause a major fissure in the crystalline structure of the calculus. Ultrasonic lithotripsy depended upon the piezo-electric effect. The endoscopic probe was really an ultrasonically driven drill that set up vibrations at the tip of the probe which then broke up the calculus into fine particles. Firm contact between the probe and calculus is needed. The probes are hollow rigid tubes through which the fragments can be aspirated with suction

Extracorporeal shock wave lithotripsy is a development of both these effects and requires no surgical intervention in most cases. The original lithotripter (Dornier) made use of the electro-hydraulic effect to generate a shock wave extracorporeally which was then focused on the stone with the aid of biplane screening. Such lithotripsy required a general anaesthetic and many thousands of stones world-wide have been successfully and non-invasively treated with such machines. Now, second and third generation machines are being developed using electromagnetic waves and ultrasound to produce the desired effect on the calculus. Ultrasonic lithotripters use an array of piezo-electric crystals in a parabola and are claimed to have a higher-frequency wave, and treatment can be tolerated by the patient without anaesthesia Two devices, the EDAP and the Wolf, are already on the market This paper aims to put into context the need of such machines, their modes of operation, the problems associated with lithotripsy and the requirement of percutaneous expertise.

## The Pathology, Investigation and Management of Non-Hodgkin's Lymphomas

**Chairman: Dr R. Buchanan**

Paper by G. M Mead. No abstract received
Paper by D. H. Wright. No abstract received

## Interventional Radiology of the Urinary Tract

**Chairman: Dr W. Hately**

Current management of urinary stones, by M. J. Kellett
Ureteric stents, by H. M. Saxton

### CURRENT MANAGEMENT OF URINARY STONES

M. J. Kellett

*Institute of Urology, London*

During the past 5 years there have been remarkable changes in the management of stone disease. Percutaneous stone extraction has been followed by extracorporeal shock wave lithotripsy. More recently, the use of laser energy for stone fragmentation has added to the variety of techniques available. Best results in stone management are achieved by a team with expertise in all these techniques. The advantages and drawbacks of these new methods of treatment are reviewed.

### URETERIC STENTS

H. M. Saxton

*X-ray Department, Guy's Hospital, London*

Upper urinary tract stenting is a valuable adjunct in the management of chronic obstruction. Indications for stenting include neoplastic occlusion, traumatic or operative stricture, and/or fistulae. Stents may be introduced via a cystoscope or percutaneously: the percutaneous route is particularly useful when there is severe narrowing, irregularity or kinking and manipulation of guides or catheters is required. Each stage of stenting—puncture of the collecting system, manipulation through tortuous ureters, passage through the narrowed area and introduction of the stent—may give rise to difficulty. These difficulties and the means of overcoming them are discussed.

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## Radionuclide Imaging at the District General Hospital

**Chairman: Dr V. B. Batty**

Brain imaging, by P. R. Camm
Heart imaging, by J. L Francis
Lung imaging, by S. J. Walkden
Indium-111 leucocyte scanning in a district general hospital and the use of an on-call service, by A J Coakley and P. J. Mountford

### BRAIN IMAGING

### P. R. Camm

*Department of Radiology, Dorset County Hospital, Dorchester, Dorset*

This paper reviews the indications and clinical use of radionuclide brain imaging and assesses the possible uses of the new brain imaging agent $^{99}$Tc$^{m}$-HM-PAO.

### HEART IMAGING

### J. L. Francis

*Department of Nuclear Medicine, Staffordshire General Infirmary, Stafford*

The contribution of nuclear medicine to diagnosis in cardiology is discussed along with the interaction between a clinical and a service department.

### LUNG IMAGING

### S. J. Walkden

*Department of Radiology, Poole General Hospital, Dorset*

The impact of the introduction of ventilation imaging with $^{81}$Kr$^{m}$ on a district general department of nuclear medicine is discussed.

### INDIUM-111 LEUCOCYTE SCANNING IN A DISTRICT GENERAL HOSPITAL AND THE USE OF AN ON-CALL SERVICE

### A. J. Coakley and P. J Mountford

*Department of Nuclear Medicine, Kent & Canterbury Hospital, Canterbury*

Indium-111 leucocyte scanning is a well established technique for identifying soft-tissue infection and is also used in the evaluation of bone sepsis. The facilities and staff implications of establishing a service at a district general hospital are discussed and the provision of an on-call service at weekends described.

Cell labelling has been performed aseptically in a Perspex glove box (100 cases), in a laminar flow cabinet (200 cases) and currently is performed in Amercare enclosures. We have found that leucocyte labelling can be performed with high efficiency by any member of staff who has undergone basic training in the technique Technicians and radiographers normally carry out labelling as part of their routine duties. Because of clinical urgency in many cases, a limited weekend on-call service has been provided (Saturday and Sunday mornings) Over a 1-year period 12 urgent leucocyte scans were performed at weekends; of these, 10 were imaged on Saturdays (*i.e.* Friday labellings) and two labellings were requested over weekends. Any department with basic radiopharmacy facilities is capable of offering indium-111 leucocyte scanning—departments without elaborate sterile enclosures should not be inhibited from introducing the investigation while awaiting improvement of facilities. To make the procedure routinely available, it is recommended that several members of staff are trained in leucocyte labelling and technical staff are available to image on Saturday mornings; urgent labelling over weekends has only rarely been requested

## History of Radiology

**Chairman: Dr J. M. Guy**

Cryptoscopy: the early history of fluoroscopy, by A. M. K. Thomas
Radiotherapy before Hiroshima· a surgical specialty in radiology? By C. C. S. Murphy
Thurstan Holland, Liverpool 1896, by A. Carty
Up the Khyber with a gas tube—early forays in military radiology, by J M. Guy
Orthodox and unorthodox uses of radioactive substances, by J. R Morgan

### CRYPTOSCOPY: THE EARLY HISTORY OF FLUOROSCOPY

### A. M. K. Thomas

*Department of Radiology, Hammersmith Hospital, London*

In 1895 Roentgen discovered the action of X rays by observing their power to illuminate a fluorescent screen and was able to visualise his own hand. In the early years of radiology fluoroscopy was the most important technique for the examination of the viscera, and it was not until after the First World War that the major technical problems of film radiography were solved. Compared with radiography, fluoroscopy involved a considerable saving of time, but often at the expense of a considerable radiation dosage to the operators This paper is a review of aspects of the early history of fluoroscopy, illustrated by work of the pioneers of radiology

# *Proceedings of The British Institute of Radiology*

## RADIOTHERAPY BEFORE HIROSHIMA: A SURGICAL SPECIALTY IN RADIOLOGY?

Caroline C S. Murphy

*Centre for the History of Science, Technology and Medicine, Department of Science and Technology Policy, University of Manchester*

Radiotherapy can be said to be as old as the practice of taking the waters at springs of slightly radioactive mineral waters, but it is perhaps more usual to think of it as an offshoot of diagnostic radiology. While there has always been a minority of radiologists who have concentrated on therapy rather than diagnosis, this paper is concerned with showing the way in which surgeons who had taken up radium therapy succeeded in establishing radiotherapy in Britain as a separate specialty from diagnostic radiology.

The first people employed in hospitals as "radiotherapists" were radium officers in pre-War independent radium institutes. X-ray therapy gained a very bad name in the early 1920s after the introduction of the dangerous Erlangen technique, but radium therapy benefited from Medical Research Council support and gained acceptance as an alternative to surgery in the treatment of certain cancers. As a result, a national radium supply was purchased and supplied to the National Radium Centres staffed with radium officers, some of whom were radiologists, some surgeons and some both. However, many surgeons continued to apply radium themselves—which could be extremely dangerous. The development of radium beam therapies just before the War undermined the surgeon's claims to control of radium therapy, as surgery was no longer needed for the application of radium tubes. By then, however, the influential surgeons who had also qualified as radiologists and established a separate society for radiotherapists. The radiotherapists and radiodiagnosticians then joined to form the Faculty of Radiologists. In consequence, when the NHS was established radiotherapy and radiodiagnosis both had specialty status in the new hospital system.

## THURSTAN HOLLAND, LIVERPOOL 1896

Austin Carty

*Department of Radiology, Royal Liverpool Hospital*

Dr C. Thurstan Holland, a general practitioner aged 33 years in 1896, set up an X-ray department in the Royal Southern Hospital, Liverpool, in June 1896 He was sponsored and generally supported in this by Robert Jones, the famous orthopaedic surgeon. From original images and clinical records made by Holland and in my possession, I have prepared an account of the very wide range of X-ray examinations carried out in the first 6 months (over 200 cases) and the remarkable prospective self-assessment established from the very beginning. Early workers in other centres tended to work in physics departments but this was one of the first, if not *the* first, X-ray units set up within a hospital.

## UP THE KHYBER WITH A GAS TUBE—EARLY FORAYS IN MILITARY RADIOLOGY

J. M. Guy

*Department of Radiology, Yeovil District Hospital, Yeovil, Somerset*

One of the earliest radiographs to be shown in Britain was of a projectile in the wrist, and it was obvious to doctors from the earliest days of medical radiology that the detection of bone injuries and bullets made imperative the diagnostic use of X rays for the wounded. The first military use was in Italy, but British military and civilian surgeons soon followed their example, in Greece, India, the Sudan and South Africa. Their preoccupations were the weight and fragility of the apparatus, possible power supply, darkness for fluoroscopy and developing, and clean water. All of these determined whether radiographs would be taken at the front or in a base hospital Experience in these early campaigns was valuable in World War I, when diagnostic radiology came into its own for the first time Contemporary photographs illustrate the way in which these difficulties were overcome. The proven usefulness of radiology stimulated its growth in Britain, particularly as a result of experience gained in the Boer War and World War I.

## ORTHODOX AND UNORTHODOX USES OF RADIOACTIVE SUBSTANCES

Jeffery R. Morgan

*Medical Department, UK Atomic Energy Authority, Harwell*

This paper reviews the role of radioactive substances as medicinals in the context of shifting attitudes to radiation of both the medical profession and the general public

As long ago as the mid 19th century, many years before the appreciation of all its physical properties, uranium was being used experimentally in a variety of medical conditions The therapeutic possibilities of radium were enthusiastically taken up following its preparation at the close of that century and several ingenious delivery systems devised to extend its clinical application. Some doctors were later to embark on a flirtation with radon therapy. All this interest by the professionals was reflected in a growing popularity for "home cures", available commercially without prescription, which claimed efficacy on account of their purported radioactivity. Spas whose waters were radioactive set out to increase their patronage with the introduction of new facilities to exploit this resource. During the late 1920s substantial medical evidence for the harmfulness of incorporated radioactivity became available. Radioactive materials for use in the home continued to be marketed in Britain until after the War, while today, at many radioactive spa treatment centres throughout the world, patients are being admitted at their physician's request.

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# Management, Computing and General Clinical

**Chairman: Professor B. S. Worthington**

Microcomputer-based departmental ordering system, by H. M. Norwood and A. J. Hall
Tendering for an X-ray computed tomography scanner, by S. Edyvean and B. J. Perry
The effect of quality assurance concepts on the organisation of patient care in a radiotherapy department, by J. A. Garrett, H. Eckert, T. J. Godden and B. J. Sholl-Evans
Use of radiology in psychiatry, by A. J. White and B. Barraclough

## MICROCOMPUTER-BASED DEPARTMENTAL ORDERING SYSTEM

H. M. Norwood and A. J. Hall

*Medical Physics Department, St James's University Hospital, Leeds*

The National Health Service is currently engaged in improving the management of finance and resources and this will undoubtedly be done using large computer systems to provide information regarding departmental expenditure. In the interim, however, many departments will feel the need to improve the financial information available to them by way of total orders placed and costs per department, etc., so that they can utilise their resources more effectively. We have adopted the "Masterfile" data base running on a BBC microcomputer to produce such information. It accepts order information that is generated from a front-end program which prints orders or requisitions on appropriate stationery. This program automatically accesses the data base and also records the supplier, brief details of the goods or services, total cost, the cost centre code to be charged and date of placing the order, etc. The facilities of the data base can then be used to manipulate such raw data to produce meaningful management information. This paper briefly describes the operation of the system, including the design of the front-end program and the modifications to Masterfile, and discusses in some detail the experience gained from using it on a day-to-day basis.

## TENDERING FOR AN X-RAY COMPUTED TOMOGRAPHY SCANNER

S. Edyvean and B. J. Perry

*Department of Medical Physics & Bioengineering, St George's Hospital, London*

Early computed tomography (CT) scanners arrived on site with even the manufacturer hardly knowing how well they performed. However, once there was competition in the market place questions had to be asked about imaging performance as well as the usual X-ray and engineering parameters. The first tendering documents asked these questions with little hope of getting full or even accurate answers. Manufacturers soon learnt what had to be said (and measured) and in response the tendering documents increased in scope, became more detailed and included specific numerical statements of the performance required. Today specification documents may run to 30 or more sections with over 350 questions to be answered or statements made. No tendering document is perfect. Once put to the test the pitfalls in any specification rapidly emerge, pointing to areas of ambiguity and questions that could be rephrased. Much of the data in the manufacturers' replies is not in a standard form and is difficult to compare. The problem areas include the presentation of scan reconstruction and scan cycle times, the practical details of dynamic scan sequences in relation to tube loading, the variations of phantom size and surface dose in contrast-detail measurements, the parameters used to characterise the modulation transfer function and the relationship of all these, and other, parameters to the scanning of typical clinical conditions. These difficulties prompt the question of whether such lengthy and detailed specifications are necessary and whether they help or hinder the scanner selection process. Could it be that scanners today are so similar in performance that such a time-consuming and complicated exercise could be abandoned? This paper highlights some of the problems the authors have found, discusses the questions raised, suggests some answers and perhaps points a way forward.

## THE EFFECT OF QUALITY ASSURANCE CONCEPTS ON THE ORGANISATION OF PATIENT CARE IN A RADIOTHERAPY DEPARTMENT

J. A. Garrett, H. Eckert, T. J. Godden and B. J. Sholl-Evans

*Bristol Radiotherapy and Oncology Centre*

Current budgetary restraints in the National Health Service have increased our awareness of the need for cost-effective methods of treatment. This has provided a stimulus to investigate ways of improving the efficiency of the radiotherapy service without impairing the quality of care. A multidisciplinary team has met regularly and examined, in a systematic and analytical manner, the interaction of all the interdependent factors which relate to the satisfactory treatment of radiotherapy patients. The group set organisational objectives and standards by which satisfactory care could be defined, with a view to determining the potential benefits which might follow from the application of quality assurance management in a radiotherapy department.

## USE OF RADIOLOGY IN PSYCHIATRY

Anthony J. White and Brian Barraclough

*Department of Psychiatry, Royal South Hants Hospital, Southampton*

A survey of the use of chest and skull radiology on patients admitted to a district general hospital adult psychiatry unit suggested overuse. As well as being published in the literature, the findings were discussed at meetings and tutorials within the unit, but no set guidelines or code of practice were issued. Two years later we repeated the survey to examine any change in practice. For chest radiographs, use fell from 31% (231 of 746 admissions) to 13% (136 of 1007 admissions) and the percentage reported as abnormal increased from 9% to 24%, a rise from 2.8% to 3.2% of all admissions. Skull radiography decreased from 7% (111 of 1691 admissions) to 4% (38 of 1007 admissions); the percentage of examinations and of all admissions reported as abnormal was constant at 2% and 0.1%, respectively. Use of computed tomography (CT) head scans increased from 0.8% (13 of 1691 admissions) to 3.3% (33 of 1007 admissions) and the percentage of examinations reported as abnormal increased from 31% to 36%, a rise from 0.2% to 1.2% of all admissions.

The findings of our two surveys suggest that, for psychiatric inpatients aged 16–65 years, in addition to the usual medical indications, a chest radiograph is indicated only when there are relevant positive clinical findings and a CT head scan when there is evidence of either organic disease of the central nervous system above the foramen magnum or a primary malignancy elsewhere. There do not seem to be any indications for skull radiographs

## Clinical: Lung

**Chairman: Dr J. E. Adams**

Pulmonary tuberculosis: patterns of presentation in the west of Glasgow 1985–86, by M. D Cowan and C Campbell

The distribution of pulmonary shadowing in farmer's lung, by P G Cook, I P. Wells and C R McGavin

Computed tomography in pleural mesothelioma, by R. M. Blaquiere and R E English

The value of computed tomography of the chest following treatment for Hodgkin's disease, by C W Heron, J. E. Husband, M P Williams and G. R Cherryman

Does inhalation of 100% oxygen reduce the incidence and severity of pneumothorax following needle biopsy of the lung? A randomised controlled study, by P. J. Shorvon, R B Pridie and D. Patel

### PULMONARY TUBERCULOSIS: PATTERNS OF PRESENTATION IN THE WEST OF GLASGOW 1985–86

M. D. Cowan and C. Campbell

*Department of Diagnostic Radiology, Western Infirmary, Glasgow*

Pulmonary tuberculosis has played a conspicuous part in the medical history of many of Britain's industrial cities, and this is particularly true of Glasgow Although the prevalence of the disease dropped sharply after the introduction of effective antituberculous chemotherapy, complete eradication of pulmonary tuberculosis has not been achieved. Since it is a treatable condition, accurate and early diagnosis is important and the radiologist has a vital part to play Patterns of presentation vary, depending on the interplay between the virulence of the organism and the resistance of the host. As well as "individual" resistance, "community" resistance is of importance and is influenced by a variety of factors, including a changing ethnic mix and alterations in immunisation practice. All the cases of pulmonary tuberculosis presenting in the west of Glasgow in 1985 and 1986 have been analysed The modes of clinical and radiological presentation are described, with particular reference to "usual" and "unusual" patterns of presentation in different age groups It is hoped that these findings will help to alert radiologists to the present spectrum of radiological presentation of pulmonary tuberculosis and so reduce the risk of misdiagnosis of a condition which usually responds well to treatment.

### THE DISTRIBUTION OF PULMONARY SHADOWING IN FARMER'S LUNG

P. G. Cook, *I. P. Wells and †C. R. McGavin

*Department of Radiology, Freedom Fields Hospital, Plymouth, *Department of Radiology, Derriford Hospital, Plymouth and †Plymouth Chest Clinic*

The clinical and pathological features of farmer's lung are well established. There is, however, less consistency in the reports of the radiological features. Although the type of shadowing seen in the acute, subacute and chronic stages have been described and are generally accepted, the distribution of the subacute-stage shadowing has been described variously by many authors. The discrepancy between the distribution of shadowing in the acute and subacute stages and that in the chronic stage has also been difficult to explain. Several cases of farmer's lung are briefly reviewed and the factors which may be involved in the production of the shadowing in the various stages are discussed in the light of recent research into the behaviour of inhaled particles, in order to help clarify the apparent discrepancy present in the literature.

### COMPUTED TOMOGRAPHY IN PLEURAL MESOTHELIOMA

R. M. Blaquiere and R. E. English

*Radiology Department, Southampton General Hospital*

A history of previous exposure to asbestos is common in patients presenting with pleural disease in south Hampshire Both patients and physicians are aware of the risk of malignancy but the diagnosis of pleural mesothelioma can be difficult. For this reason we reviewed the thoracic computed tomography (CT) findings in 19 consecutive patients who were suspected of having malignant mesothelioma and who later proved to have the disease. Bone destruction and diaphragmatic invasion were regarded as signs diagnostic of malignancy. Additional signs such as the depth, character and extent of the pleural change were quantified and identification of soft-tissue or lung infiltration was attempted. A number of other features such as pleural effusion, contraction of the hemithorax and the presence of pleural calcification were noted. It was found that in pleural mesothelioma 95% of patients had diffuse, irregular pleural thickening with a mean depth of 2 cm. There was involvement of multiple pleural surfaces in 90% of the patients. In 79% there was evidence of direct local tumour invasion or infiltration.

Law et al (1982) showed that in patients with known mesothelioma being assessed for treatment, CT offered little advantage over conventional chest radiographs. However, these authors and Rabinowitz et al (1982) agreed that CT showed the features of pleural disease more graphically than conventional methods. Grant et al (1983) and Mirvis et al (1983) found CT useful for staging mesothelioma as well as assessing the therapeutic response, while Libshitz (1984) described an additional role for CT in the differential diagnosis of pleural malignancy. We have found CT most useful in making the initial diagnosis of a malignant pleural process. However, the CT findings can also prove invaluable in the day-to-day management of the patient, even though the therapeutic options are somewhat limited. In addition, our surgeons have found CT useful in the pre-operative assessment of the patient being considered for pleurectomy

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### THE VALUE OF COMPUTED TOMOGRAPHY OF THE CHEST FOLLOWING TREATMENT FOR HODGKIN'S DISEASE

C. W. Heron, J. E. Husband, M. P. Williams and G. R. Cherryman

*CRC Radiology Research Group, Royal Marsden Hospital, Sutton, Surrey*

The value of computed tomography (CT) in the staging of patients with Hodgkin's disease is well established, but its role in the subsequent assessment of patients is less clear. A retrospective review of chest CT scans of patients with Hodgkin's disease performed for reasons other than primary staging was undertaken. The purpose of the review was to determine the reasons for scanning and to assess the significance of results. Ninety scans were reviewed and 40 CT examinations were performed to assess response to treatment In four of these, mediastinal disease had been demonstrated by CT only. Fifty scans were performed to evaluate the mediastinum and lung parenchyma in known or suspected relapse. Computed tomography and plain radiography agreed in 26 of these, with CT providing additional information in seven. Computed tomography was especially useful in the remaining 24 patients, in whom the mediastinum appeared abnormal on chest radiographs following therapy, making it difficult to distinguish radiation changes from recurrence. Computed tomography was true positive in 11 cases, true negative in 12 and false positive in one Parenchymal abnormalities were demonstrated by CT in nine patients In four scans, more lesions were seen on CT than on plain radiographs and in two CT enabled differentiation of post-therapy change from parenchymal Hodgkin's disease

### DOES INHALATION OF 100% OXYGEN REDUCE THE INCIDENCE AND SEVERITY OF PNEUMOTHORAX FOLLOWING PERCUTANEOUS NEEDLE BIOPSY OF THE LUNG? A RANDOMISED CONTROLLED STUDY

P. J. Shorvon, R. B. Pridie and *D. Patel

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Pneumothorax is the commonest potentially serious complication following lung needle biopsy A previous study (Cormier et al, 1980) suggested that 100% oxygen inhalation reduces the severity and incidence of pneumothorax because of the increased absorption rate of oxygen compared with nitrogen To test this hypothesis we performed a controlled trial of consecutive patients referred for lung needle biopsy to Harefield Hospital. Patients hypercapnoeic at rest ($P_{CO_2} > 6.6$ kPa) or with severe pulmonary hypertension were excluded from trial The remainder were randomised to receive either 100% oxygen (Group A) or air (Group B) via a face mask for 5 min before, during and 10 min after the procedure. All biopsies were performed by one operator (R P.) unaware of which gas was being administered All patients had expiratory chest radiographs immediately after and 24 h after the procedure Clinical data, pathological findings and follow-up information were recorded prospectively. At the end of the study, before the randomisation code was broken, all the radiographs were reviewed by two radiologists (R.B.P. and P.J.S.) and agreement reached on the presence and size of any pneumothorax identified Fifty-one patients were randomised to Group A and 48 to Group B The incidence of pneumothorax was not significantly different· Group A 15 of 51 patients (28%), Group B 13 of 48 (27%). Chest drain insertion was required clinically in two patients in each group. The average size of the pneumothoraces was not significantly different between the groups either immediately or at 24 h Six pneumothoraces were visible only on the later radiograph (four in Group A, two in Group B). The most significant factor in the production of a pneumothorax appeared to be the number of passes of the needle: eight of the 20 (40%) patients who underwent more than one pass developed a pneumothorax compared with 18 of the 79 (22%) who had one pass It is concluded that 100% oxygen therapy is of no value in reducing the incidence or severity of pneumothorax.

### REFERENCE

CORMIER, Y., LAVIOLETTE, M. & TAROIF, A., 1980 *Thorax, 35,* 37–41.

## Royal College of Radiologists George Simon Lecture (sponsored by Picker International)

### RADIOLOGY AND CYSTIC FIBROSIS

John C. Batten

*Formerly of Department of Thoracic Medicine, Brompton Hospital, London*

The experience gained over the last 25 years in the Department of Cystic Fibrosis at the Brompton Hospital is presented. The cases of more than 350 adolescent and adult patients form the basis of the lecture.

Criteria for the diagnosis are reviewed and the main feature of the lecture is the use of imaging techniques, especially conventional radiography, in the management of the disease The radiological changes in the lung are described, with illustration of the wide variation in severity, the response to treatment of the bronchopulmonary disease and its progression to cardiorespiratory failure. Complications such as allergic bronchopulmonary aspergillosis, mycobacterial disease, haemoptysis and pneumothorax are discussed and skeletal changes illustrated The use of radiology and ultrasound to demonstrate the abdominal features and complications are outlined, in particular those associated with distal intestinal obstruction syndrome (meconium ileus equivalent). Other complications which affect the duodenum, liver, gallbladder and pancreas are mentioned Neoplasia of clinical and pathological interest has presented interesting radiological abnormalities including changes seen on computed tomography

## Perspectives of Quality in Radiology

**Chairman: Mrs M. J. Harvey**

Introduction, by M. J. Harvey
What is quality and whose is it? By D A High
The provider's view
The radiologist, by R. J. Burwood, N. L. Bishop and J Lutkin
The radiographer, by J. R. L. Nettle
The consumer's view
The clinician, by M. E. Shipley. No abstract received
The patient, by I. Candy
The manager's view, by I Donnachie

### INTRODUCTION

M. J. Harvey

*Middlesex Hospital, London*

The assurance of quality in health care is a prime objective for all those working within the health service today. Quality assurance programmes are being established within health authorities in order to evaluate and monitor the standard of care provided. As a part of these programmes, the work and performance of the diagnostic radiology department is beginning to be assessed and evaluated

People's perception of what constitutes a quality radiology service depends on their relationship to the service. The providers of this service are influenced primarily by professional standards and their needs for job satisfaction, whereas the referring clinician's view will be dominated by his need to obtain accurate and relevant diagnostic information about his patient. Patients have their own, often different perspective of a radiology service, their view of quality being mainly determined by individual experience As the general public becomes better informed their expectations and demands will continue to increase and become more sophisticated The health service manager has to consider the quality of the radiology service as a part of the total health care package in meeting the needs not only of individual patients but also of the local community

Traditionally, interest in quality assurance in radiology has focused on technical issues, *e g.* about the effectiveness and reliability of X-ray equipment. This seminar is designed to develop a more comprehensive view of quality in radiology by approaching the subject from the perspective of the shareholders—providers, consumers and management.

### WHAT IS QUALITY AND WHOSE IS IT?

D. A. High

*Paddington and North Kensington Health Authority, London*

See introduction

### THE PROVIDER'S VIEW: THE RADIOLOGIST

R. J. Burwood, N. L. Bishop and *J. Lutkin

*Departments of Radiology and *Medical Physics, Royal Sussex County Hospital, Brighton*

In 1984 a structured Quality Assurance programme was introduced to cover all aspects of activity within the Brighton Health District. The formal committee structure and its function are described and some aspects of clinical resistance are discussed. Activity within the "Radiological Services Quality Assurance Body" since its inception on September 1, 1984 is reviewed.

### THE PROVIDERS' VIEW: THE RADIOGRAPHER

Jeremy R. L. Nettle

*Department of Diagnostic Imaging, Salisbury General Infirmary, Wiltshire*

Quality may be defined in an imaging department as the effective use of financial and manpower resources in maximising health care, thus providing a consistent performance in customer service. The quality of the service will depend upon such factors as environment, recruitment, training and development, communication, and feedback The quality of a service department is dependent on the basic fundamentals of "getting it right".

### THE CONSUMER'S VIEW: THE PATIENT

Irene Candy

*Southampton and South West Hampshire Health Authority*

I feel that, as a patient, I must be able to take it absolutely for granted that the treatment or diagnosis I am offered will be of the best possible quality for its purpose. I must have this trust because I have no personal technical understanding of, or control over, what is going on. I am, however, handing over my most treasured possession, my body, to the ministrations of other people and I need to be sure that I am "properly treated" in all senses of the phrase. My requirements, listed below, are simple

(1) I should be pleasantly and kindly received and accommodated whilst waiting and should know in advance how long that wait will be, and how long my treatment/diagnosis will take
(2) I should have my fears allayed when confronted with complex, frightening and perhaps overwhelming equipment
(3) I should have carefully explained to me, at each stage of the proceedings, what is being done and why, and to have this done in a way I can understand, and to be able to ensure that I *do* understand by asking questions and having them answered as fully and truthfully as possible.
(4) I should know what the next step will be in my treatment—how long it will be before I am seen again

Before I make my contribution on behalf of patients, to the Congress, I intend to do some reasearch among patients attending clinics in Southampton, to see how far my own perceptions are shared and how far expectations are met In the light of this, I may need to add to my list.

### THE MANAGER'S VIEW

Ian Donnachie

*St James' University Hospital, Leeds*

Can the genuine concerns of staff survive the avalanche of damage resulting from the "QA hit squads" wandering aimlessly across the health service? Service quality must remain a central concern of all staff, not just the "have a nice day" brigade Management has failed to exploit staff instead, it has ignored them. How many diagnostic radiology departments exhibit "dynamic indifference" towards patients—how long they wait, their dignity? And staff—many bright young staff must be "talent spotted" and their initiatives and enthusiasm fully exploited. Quality and quantity are uneasy bedfellows—the "quicker, slicker, but sicker" approach is induced by crude measures of service provision. Workload and revenue impact on clinical support departments arising from consultant appointments must be addressed

## Clinical. Neurology, Cardiology and Vascular

**Chairman: Professor B. S. Worthington**

The evaluation of cerebral vascular disease using technetium-labelled HMPAO, X-ray computed tomography and magnetic resonance imaging, by F. W Smith, P. F. Sharp, H. G Gemmell and N T. S Evans

Technetium-99m HMPAO a new cerebral blood flow agent for the investigation of dementia, by H. G Gemmell, F W. Smith, J. A O Besson, P. F Sharp and N. T S Evans

Computed tomography of the brain in small-cell lung cancer, by G R Cherryman, L Maclean, M Vincent, C W. Heron, M P Williams, I E Smith and J E Husband

The role of magnetic resonance imaging in the recognition of giant intracranial aneurysms, by T Jaspan, B. S Worthington and I. Holland

A comparative study of magnetic resonance imaging and computed-tomography-assisted myelography in spinal dysraphism, by T. Jaspan, B S. Worthington and I. Holland

Initial experience with ultra-fast computed tomography for measurement of left ventricular volumes in human subjects, by R M MacMillan, F J. Lumia and M. R Rees

A simplified method for short-axis view cine computed tomography quantitation of left ventricular ejection fraction, by R M MacMillan and M R. Rees

Green Lane coronary analysis a comparison with three-vessel terminology, by A. Jones and P. Wilde

Late post-operative evaluation of ascending aortic surgery using computed tomography and ultrasound, by S Chatterjee, M Papouchado, J D Wisheart and P Wilde

Digital angiography of the pulmonary arteries in the intensive care unit, by E Mangel, R. W Kenn, R M Huber, M Haider and K. J Pfeifer

Digital subtraction angiography in children, by R. W. Kenn, E. Mangel, A Samija, R M. Huber and K J. Pfeifer

Is the internal iliac artery at risk in common and external iliac angioplasty? By A C Page and I P Wells

### THE EVALUATION OF CEREBRAL VASCULAR DISEASE USING TECHNETIUM-LABELLED HMPAO, X-RAY COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING

F W Smith, *P F. Sharp, *H. G. Gemmell and *N. T. S. Evans

*Department of Nuclear Medicine, Aberdeen Royal Infirmary and *Department of Biomedical Physics, University of Aberdeen*

Technetium-labelled hexamethyl propylene amine oxime (HMPAO) is an agent which is removed from the circulation by the cerebral grey matter Its distribution within the cerebral grey matter reflects the blood supply to the brain Thirty examinations in 28 patients with either acute stroke or transient ischaemic attack have been studied by technetium-HMPAO tomography, X-ray computed tomography (CT) or magnetic resonance imaging (MRI). In this study, 14 of the 16 patients suffering from acute stroke showed matching underperfusion with HMPAO and their CT or MRI studies The other six showed reduced cortical perfusion with the technetium HMPAO with only areas of small infarction in the internal capsule being demonstrated by CT The remaining eight patients had suffered a transient ischaemic attack and four showed no abnormality on either technetium-HMPAO tomography or CT The remaining four showed areas of cortical underperfusion with technetium HMPAO but had a normal CT examination. Follow-up of two of these cases showing cortical underperfusion demonstrated normal perfusion 1 month after the attack Technetium HMPAO is a relatively inexpensive agent for demonstrating regions of absent or underperfusion in the brain which correlates well with conventional CT findings and the clinical condition of the patient

## TECHNETIUM-99M HMPAO: A NEW CEREBRAL BLOOD FLOW AGENT FOR THE INVESTIGATION OF DEMENTIA

H. G. Gemmell, *F. W Smith, †J. A. O Besson, P. F. Sharp and N. T. S. Evans

*Departments of Biomedical Physics, *Nuclear Medicine and †Mental Health, University of Aberdeen*

One of the potential clinical uses of the new cerebral blood flow agent $^{99}$Tc$^{m}$ hexamethylpropyleneamine oxime (HMPAO) is the investigation of dementia, for example to differentiate between dementia of the Alzheimer type (DAT) and multi-infarct dementia (MID), or to study Korsakoff's psychosis (KP) and Huntington's disease (HD) Patients and three normal volunteers were imaged both with single-photon emission computed tomography (SPECT) and nuclear magnetic resonance Out of 17 DAT patients and 10 MID patients it was found that HMPAO perfusion deficits were much more common in the DAT group than in the MID group, especially in the temporo-parieto-occipital (TPO) regions. The two groups of patients were found to be significantly different ($p = 0.02$) as regards the frequency of occurrence of bilateral TPO perfusion deficits Serial studies in the DAT and MID groups are now taking place and initial results are presented. Preliminary results in the KP group showed no typical pattern of uptake but the HD group had evidence of reduced uptake in the head of the caudate nucleus with normal uptake in the cortex. Since HMPAO does not suffer from cost and availability problems it is concluded that $^{99}$Tc$^{m}$-HMPAO will play a major role in the investigation of dementia, particularly as a positive test for DAT.

## COMPUTED TOMOGRAPHY OF THE BRAIN IN SMALL-CELL LUNG CANCER

G. R. Cherryman, L. Maclean, M Vincent, C. W. Heron, M. P. Williams, I. E. Smith and J. E. Husband

*Departments of Radiology and Medicine, Royal Marsden Hospital, Sutton, Surrey*

We have found that at presentation computed tomography (CT) of the brain will detect metastases in 11.6% of our patients with small-cell lung cancer Patients continue to remain at high risk of developing cerebral metastasis We have also found that regular 3-monthly CT brain scans will detect 87% of subsequent metastases while still clinically occult. We re-examined patients who had a negative brain CT scan at presentation at 3, 6, 9 and 12 months Occult metastases were detected in none of our patients at 3 months, 13.6% at 6 months, 20% at 9 months and 16.6% at 1 year. We conclude that CT is an effective method of detecting brain metastases at presentation. The majority of subsequent metastases can be detected while still clinically occult provided CT scans are repeated at 3-monthly intervals.

## THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE RECOGNITION OF GIANT INTRACRANIAL ANEURYSMS

T. Jaspan, B. S. Worthington and I. Holland

*Department of Academic Radiology, University of Nottingham*

Although the classification of intracranial aneurysms by size is arbitrary, those with a diameter exceeding 25 mm are by convention called giant Many contain organised lamellated thrombus with only a small eccentric lumen in the aneurysm that could be opacified at angiography Most present clinically as an intracranial mass lesion rather than with subarachnoid haemorrhage Although they can be readily detected on computed tomography (CT), and their features are now well documented, attention to detail is required if a correct diagnosis is to be made Care is particularly necessary with basal para-sellar masses and extra-axial retroclival and cerebellopontine-angle masses showing calcification and an enhancement pattern simulating meningioma We have retrospectively reviewed the magnetic resonance studies in 16 cases of giant intracranial aneurysm and compared the findings with those from CT and angiography. Magnetic resonance imaging was carried out on a 0.15 T resistive system using a variety of pulse sequences and in the three orthogonal planes, and it demonstrated the vascular nature of the mass in each case without the need for contrast medium. High-velocity flow within the aneurysms was demonstrated by a flow void and slower flow was highlighted by means of an even-echo rephrasing technique. Fresh thrombus within the aneurysm after ligation of the neck could be readily identified from its high signal on inversion-recovery sequences. We conclude that magnetic resonance imaging is a reliable technique for demonstrating the presence of giant aneurysms and, except where thrombosis has completely obliterated the lumen, precise diagnosis is possible by the use of flow-dependent sequences.

## A COMPARATIVE STUDY OF MAGNETIC RESONANCE IMAGING AND COMPUTED-TOMOGRAPHY-ASSISTED MYELOGRAPHY IN SPINAL DYSRAPHISM

T. Jaspan, B. S. Worthington and I. Holland

*Department of Academic Radiology, University of Nottingham*

Spinal dysraphism embraces a spectrum of anomalies of the spine, spinal cord and thecal envelope which may be associated with congenital tumours such as lipomas and dermoid Presentation may be with lower-limb abnormalities, including inequalities of limb size or deformity and muscle wasting, or with disturbed sphincter function. A series of 25 such patients aged between 3 years and 18 years was examined on a 0.15 T resistive system and the results compared with those obtained at myelography followed by computed tomography. A variety of pulse sequences was used. A $T_1$-weighted spin-echo sequence was useful to display the overall anatomy and it gave a clear separation of cord and cerebrospinal fluid (CSF) The total CSF pool was highlighted on heavily $T_2$-weighted spin-echo sequences A combination of sequences was useful in providing a measure of characterisation of intraspinal tumours, fat giving a high signal on both $T_1$- and $T_2$-weighted sequences Imaging was carried out in the sagittal and transverse axial plane, but in scoliotic patients the coronal plane was used in preference to the former Magnetic resonance imaging (MRI) gave a clear depiction of cord anatomy and was especially useful in demonstrating an associated hydromyelic cavity. Both techniques demonstrated associated tumours with equal facility Although tethering bands could be recognised on MRI, details of root anatomy were beyond the resolving power of the system. We conclude, however, that MRI has a promising future in the evaluation of this group of disorders owing to the total avoidance of ionising radiation and the non-invasive nature of the study

## INITIAL EXPERIENCE WITH ULTRA-FAST COMPUTED TOMOGRAPHY FOR MEASUREMENT OF LEFT VENTRICULAR VOLUMES IN HUMAN SUBJECTS

R. M. MacMillan, F. J. Lumia and M. R. Rees

*Hahnemann Medical College, Philadelphia, Pennsylvania, USA and Killingbeck Hospital, Leeds*

Nine patients, mean age 65 (range 59–77) years, five men and four women, with normal left ventricular function documented by catheterisation, made up the study group Left ventricular ejection fraction by single-plane angiography was 76% (mean) (range 61–90%) Ultra-fast computed tomography (CT) was performed 1 day after catheterisation. A standard bolus of 42 ml of Renografin 76 was injected into the fasting subject through a median antecubital vein at a rate of 2–3 ml/s by a powered injector. Two consecutive eight-level r-wave triggered cine-mode scans (10 images/level) were acquired, starting above the aortic valve and continuing through the left ventricular apex End-systolic and end-diastolic images containing right (RV) and left ventricular (LV) cavity had area measured by computerised planimetry and slice volume was derived The sum of these slice volumes yields end-diastolic (EDV) and end-systolic volumes (ESV) Since endocardium/cavity edge detection is a critical variable in volume measurement, two methods of edge detection were employed Method 1 involved subjective adjustment of level and window for the sharpest cavity interface Method 2 set the window width at unity for a black and white image and adjusted the level to approximately half the difference in CT number between myocardium and contrast-filled cavity Volumes derived by CT in Method 1 and Method 2 (mean ±SD) were compared using the unpaired $t$-test and are shown with standard normal values established by biplane ventriculography at catheterisation (Table I).

TABLE I

| | Method 1 | Method 2 | Normal |
|---|---|---|---|
| LVEDV (ml/beat/m$^2$) | 47.8±15.4 | 66.3±19.9* | 70±10 |
| LVESV (ml/beat/m$^2$) | 12.1±5.0 | 21.9±9.7* | 24±10 |
| LVSV (ml/beat/m$^2$) | 35.7±12.5 | 44.2±14.6* | 45±13 |
| RVEDV (ml/beat/m$^2$) | 64.9±17.6 | 75.4±23.1† | 76±11 |
| RVESV (ml/beat/m$^2$) | 28.5±13.7 | 36.1±16.6‡ | 26±6 |
| RVSV (ml/beat/m$^2$) | 34.0±9.1 | 39.5±10.6† | 50±6 |

*$p < 0.001$, †$p < 0.02$, ‡$p =$ NS

We conclude that ultra-fast CT can be used to measure ventricular volumes and, using Method 2, can yield volumes comparable to normal values from catheterisation. Ventricular volumes derived from CT must be correlated with biplane angiography (in progress) to determine accuracy and reproducibility of this technique.

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## A SIMPLIFIED METHOD FOR SHORT-AXIS VIEW CINE COMPUTED TOMOGRAPHY QUANTITATION OF LEFT VENTRICULAR EJECTION FRACTION

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We have previously shown that left ventricular ejection fraction derived by measurement of left ventricular volumes using cine computed tomography (CT) in the long-axis planar view correlates well with catheterisation (MacMillan et al, 1985). Measuring left ventricular ejection fraction by left ventricular volumes in the short-axis planar view by cine CT requires multiple injections of contrast medium and time-consuming data analysis Twenty five patients, mean age 55 years, 21 male, with left ventricular ejection fraction ranging from 24% to 82%, had long-axis view and short-axis view left ventricular ejection fraction measured by cine CT. The long-axis view is achieved by slewing the supine patient counterclockwise 20° while the short-axis view involves slewing the patient clockwise 25° with foot-down table tilt 25°. Long-axis view left ventricular ejection fraction was measured using Simpson's reconstruction of end-diastolic and end-systolic images of the entire left ventricular cavity with resultant determination of left ventricular end-systolic and end-diastolic volumes. Short-axis view left ventricular ejection fraction was measured using two, four and six contiguous slices through the left ventricle with the most superior slice through the left ventricular base The left ventricular ejection fraction correlation between the long-axis view and the two contiguous middle slices of the six was $r = 0.87$, the first four slices starting from the base towards apex, $r = 0.82$, the distal four slices excluding the first two at the base, $r = 0.95$, and all six slices, $r = 0.93$. We conclude that for reliable measurement of left ventricular ejection fraction using the cine CT short-axis view, at least four contiguous slices through the proximal portion of the left ventricle, excluding slices through the base and left atrium, are required Unlike measurement of left ventricular ejection fraction in the long-axis view (MacMillan et al, 1986), a single slice in the short-axis view cannot be used reliably to estimate left ventricular ejection fraction

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## GREEN LANE CORONARY ANALYSIS: A COMPARISON WITH THREE VESSEL TERMINOLOGY

Angela Jones and Peter Wilde

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Coronary anatomy and pathology were analysed using the Green Lane diagram and score. Individual variations in size and distribution of all major coronary arteries are recorded The severity of stenosis and the amount of myocardium beyond each stenosis influence the score which thus reflects coronary occlusive disease affecting the whole left ventricle (LV). Arteriograms from 889 consecutive patients were reviewed. The LV myocardial distribution was anterior descending artery (LAD), 17–80% (mean 46%), circumflex artery (CX), 0–70% (mean 30%), right coronary artery (RCA), 0–53% (mean 24%). A questionnaire returned from 17 British cardiosurgical centres showed that all used "three vessel disease" terminology but there was considerable variation in interpretation. Estimates of cross-sectional area and diameter were variably used and sometimes neither was specified. The severity of stenosis classifying a vessel as "diseased" also varied. In some centres no quantitative assessment was made. The disease was, therefore, assessed using an international three vessel classification (CASS study) which defines a diseased vessel as one with a 70%-diameter stenosis (≃90%

cross-sectional area) in an operable LAD, CX or RCA. This was compared with the Green Lane score in which normal coronary arteries score 0/15 and complete occlusion of all arteries scores 15/15. Mean scores were (±standard deviation). zero vessel disease, 0.4 (±1.3); one vessel disease, 6.0 (±2.0); two vessel disease, 9.8 (±1.9), and three vessel disease, 12.9 (±0.8). There was considerable overlap of scores between adjacent groups and some overlap between zero and two or one and three vessel disease. In individual cases the overall scored severity of disease cannot be accurately described in terms of the number of diseased vessels. Three vessel terminology is, thus, an inaccurate and potentially misleading method of describing the extent of occlusive coronary artery disease.

## LATE POST-OPERATIVE EVALUATION OF ASCENDING AORTIC SURGERY USING COMPUTED TOMOGRAPHY AND ULTRASOUND

S. Chatterjee, M. Papouchado, J. D. Wisheart and *P. Wilde

*Departments of Cardiology and *Radiodiagnosis, Bristol Royal Infirmary*

A study was carried out to determine how well these non-invasive techniques could assess post-operative status. Nineteen adults with ascending aortic replacement were examined by contrast-enhanced computed tomography (CT) and ultrasound of the chest and abdomen. The interval between surgery and scanning was 1–11 (mean 5.5) years. The patients were clinically well, all being in New York Heart Association Categories I and II. Eight patients had surgery for acute and two for chronic Type 1 dissection of the aorta, six for annulo-aortic ectasia and three for aortic aneurysm due to Marfan's syndrome. Eleven patients had aortic-valve replacement, nine with a composite valve and aortic graft (including coronary reimplantation). In nine of the 10 dissection cases the CT scans showed a persisting contrast-enhanced false lumen with an intimal flap. In seven the false lumen extended from ascending to abdominal aorta. Ultrasound imaging showed an intimal flap in five, one not shown on CT. No false lumen or flap was shown in any other case. In these 10 dissection cases there were two composite aortic-valve replacements, six valve resuspensions and two valves were untouched. Doppler echocardiography demonstrated aortic regurgitation in both untouched valves and three resuspended valves. The remaining nine patients all had aortic-valve replacement. One Starr-Edwards prosthesis showed regurgitation and one patient with a bioprosthesis had possible regurgitation. In two of these nine patients the contrast-enhanced graft lay in a large, non-enhanced structure, presumed to be the original aneurysm refilled with thrombus. The combination of the techniques appears very effective in demonstrating the persistent false lumen, aortic regurgitation and "false aneurysm".

## DIGITAL ANGIOGRAPHY OF THE PULMONARY ARTERIES IN THE INTENSIVE CARE UNIT

E. Mangel, R. W. Kenn, R. M. Huber, M. Haider and K. J. Pfeifer

*Rontgenabteilung der Medizinischen und Chirurgischen Klinik, Innenstadt der Universität München, West Germany*

The extent of obstruction, early diagnosis and the commencement therapy are very important for the prognosis of acute embolism of the pulmonary arteries. Angiography or scintigraphy is only possible in special radiological departments. In this life-threatening situation, the patient under artificial ventilation has to be examined by angiography in the intensive care unit. We injected contrast medium via a pulmonary catheter. Video recordings, taken by a mobile C-arrow, were digitised and subtracted off-line by a computer. We found in all (nine) patients an embolus of the central pulmonary artery. In comparison with digital subtraction angiography, the disadvantage is the high degree of image noise and the small diameter of the mobile C-arrow. Despite this we were able to detect central embolism, even in re-animation.

## DIGITAL SUBTRACTION ANGIOGRAPHY IN CHILDREN

R. W. Kenn, E. Mangel, A. Samija, R. M. Huber and K. J. Pfeifer

*Department of Radiology, Chirurgische und Medizinische Klinik, Innenstadt der Universitat München, West Germany*

Digital subtraction angiography is a routine diagnostic method in adults. In children, special difficulties are limited co-operation, short transit times and different injection sites. Resolution of smaller vessels is still limited. Children have to be sedated or anaesthetised in order to eliminate motion artefacts. A higher number of mask frames is necessary for optimal subtraction in different respiratory phases. Using peripheral injection, the contrast medium must be pushed with saline solution to avoid overlapping of venous and arterial filling phases. Venous injections are performed into scalp, foot or hand veins or via a central venous catheter, intra-arterial injections may be performed by advancing a transvenous catheter through the foramen ovale or via the femoral artery with a F4 catheter. Thoracic vessels can be sufficiently visualised transvenously. For abdominal vessels, an arterial approach is recommended.

## IS THE INTERNAL ILIAC ARTERY AT RISK IN COMMON AND EXTERNAL ILIAC ANGIOPLASTY?

A. C. Page and *I. P. Wells

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It has recently been suggested that specific measures should be taken to preserve the internal iliac artery origin during angioplasty of the common and external iliac arteries around the iliac bifurcation. This study has been conducted to assess the effects on the internal iliac artery origin of angioplasty around the iliac artery bifurcation. Sixteen patients who had recently undergone angioplasty in these areas have been studied. Fifteen patients had stenoses and one a short occlusion. All the patients had lower-limb claudication and had patent internal iliac arteries before angioplasty. Post-angioplasty angiograms were performed on all patients and clinical follow-up has been for at least 1 year. There has been no clinical or angiographic evidence of compromise of the internal iliac artery on the side of the angioplasty in any of the patients in this study. As a result, we do not undertake any specific measures to preserve the internal iliac artery origin when conducting common or external iliac angioplasty.

## Posters. Clinical: Lung and Breast

**Chairman: Dr C. Flower**

The radiological features of histologically proven bronchoalveolar-cell carcinoma. A review of 18 cases, by L N Sutton, J. F. J Morrison and M. R Rees

*Pneumocystis carinii* infection in AIDS: correlation between radiography and clinical signs, by E Mangel, R. Huber, A. Pforte, A Witte and K J. Pfeifer

Spontaneous neonatal pneumothorax and pneumomediastinum, by J. J. Langham-Brown and I Hyde

Depressed sternum revisited, by C. S Ward and A G Wilson

Computer-aided analysis of the spatial relationships of grouped microcalcifications in breast disease, by D. M Hansell, J. C. Cooke, C. A Parsons and S H. Evans

### THE RADIOLOGICAL FEATURES OF HISTOLOGICALLY PROVEN BRONCHOALVEOLAR-CELL CARCINOMA. A REVIEW OF 18 CASES.

L. N. Sutton, *J. F. J. Morrison and M. R. Rees

*Department of Radiology and *Respiratory Function Laboratory, Killingbeck Hospital, Leeds*

Eighteen fully documented cases, 13 male and six female (mean age 65, range 47–78 years), of broncho-alveolar-cell carcinoma out of 43 listed by the Yorkshire Regional Cancer Organisation (from a population of four million) for the period 1975–1986 are discussed. Predominant chest radiological features at presentation were: single 3 cm nodule, one case, large mass, three cases; focal persistent segmental/lobar consolidation, six cases; coarse, widespread nodules, two cases, diffuse alveolar shadowing, one case, with focal consolidation three cases, and multifocal persistent consolidation with alveolar shadowing, two cases. Five cases (28%) presented with bilateral, 12 cases (66%) with right lung and only one case with left lung involvement An air bronchogram was detected in all but four cases. Other coexisting features were volume loss (three cases), interstitial lines (four cases) and pleural effusion (one case) No bone metastases were seen Seven patients with focal disease underwent thoracotomy, two of whom showed no evidence of recurrence 10.5 years and 4.5 years after surgery. Mean survival time without surgery was 102 (range 8–224) days. In all cases there was a progression to bilateral chest shadowing and either predominantly multinodular or multifocal consolidation with areas of alveolar shadowing The severity and duration of presenting symptoms (dyspnoea and productive cough) bore no relation to radiological findings. Pleuritic chest pain was present in five cases. In general, chest radiography findings at presentation were florid and symptoms relatively slight. However, prognosis did depend on the radiographic findings, a single nodule or mass carrying the best prognosis and bilateral disease at presentation the worst

### *PNEUMOCYSTIS CARINII* INFECTION IN AIDS: CORRELATION BETWEEN RADIOGRAPHY AND CLINICAL SIGNS

E. Mangel, R. Huber, A. Pforte, A. Witte and K. J. Pfeifer

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The acquired immunodeficiency syndrome is accompanied by infectious pulmonary and gastrointestinal complications. We compared sequences of chest radiographs with clinical findings, blood-gas analysis, pulmonary function and microbiological results Most patients died in respiratory failure The analysis of disease progression showed correlations of clinical and radiological findings. In the beginning of the *pneumocystis carinii* infection only discrete, fine reticular signs were seen radiographically, despite grave clinical symptoms with impaired pulmonary function In the further course of the disease, with additional infection and alveolar involvement, radiography also showed confluent infiltrations The demonstration of these typical radiographic findings is of essential value in the early diagnosis of *pneumocystis carinii* infection

### SPONTANEOUS NEONATAL PNEUMOTHORAX AND PNEUMOMEDIASTINUM

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The incidence of spontaneous neonatal pneumothorax and pneumomediastinum is in the order of one to three per 1000 live births and accounts for 40% of all neonatal pneumothoraces, the remainder occurring in infants receiving mechanical ventilation for underlying respiratory disorders, usually hyaline membrane disease If the diagnosis of spontaneous pneumothorax can be confidently made from the chest radiograph the child ceases to be a cause of concern, as most of these air leaks close spontaneously and do not require drainage. However, the radiograph for this condition may be misinterpreted and the child then subjected to inappropriate investigation or treatment Correct diagnosis is utterly dependent on high-quality radiographs and this requires suitable equipment, capable of producing short exposure times and with a small focal-spot tube, and careful radiographic technique However, either false positive or false negative misinterpretations may be made.

*False negative interpretation* as the patients are usually examined in the supine position, air may collect in unusual places compared with the erect radiograph, *e g* anterior, inferior or medial to the lung, producing subtle or bizarre abnormalities This is particularly so when there is an associated pneumomediastinum, when the thymus is elevated to the thoracic apices

*False positive interpretations* There are several causes of lines and apparent translucencies on the neonatal chest radiograph that may be mistaken for a pneumothorax· skin folds, scapular edge, anterior end of the greater fissure, external artefacts, sternal recession and rotation Cases are demonstrated that illustrate the features mentioned in this presentation.

### DEPRESSED STERNUM REVISITED

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Depressed sternum was first assessed radiologically by Groedel in 1911. Subsequent attempts to characterise the features of sternal depression on the postero-anterior chest radiograph have depended on uncontrolled and often small series We have therefore reassessed the value of various described signs in a controlled series. The postero-anterior and lateral chest radiographs of 50 unselected patients with sternal depression, together with 50 age-matched controls, have been reviewed The features assessed included position of the cardiac silhouette, heart size, contour of the left heart border and main pulmonary artery and right lower zone radiodensity. In addition, a number of measurements of rib configuration were made The degree of sternal depression was determined from the lateral chest radiograph. The sensitivity and specificity of the various signs described on the postero-anterior chest radiograph have been evaluated and related to the presence or absence of sternal depression and its severity

### COMPUTER-AIDED ANALYSIS OF THE SPATIAL RELATIONSHIPS OF GROUPED MICROCALCIFICATIONS IN BREAST DISEASE

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Grouped microcalcifications as the sole abnormality on a mammogram pose a diagnostic problem since they may represent either benign or malignant breast disease. Many authorities have stated that there is a subjective difference in the disposition of microcalcifications in benign and malignant breast disease The mammograms of 444 patients who had a breast biopsy leading to a definitive histological diagnosis were reviewed. In 21 cases (4 7%) grouped microcalcifications were identified as the only mammographic abnormality These groups were analysed to determine whether there was any quantitative difference between benign and malignant lesions with respect to the shape parameter of the group, the spatial frequency of the particles and neighbour-to-neighbour relationships of the microcalcifications This computer-aided analysis did not reveal any significant difference between the spatial relationships of the grouped microcalcifications found in benign and malignant breast disease.

## Posters. Clinical: Abdominal and Musclo-Skeletal

**Chairman: Dr D. Rickards**

Image quality of abdominal computed tomography in the elderly, by J Baldwin, P Sharpe, S Cole and A K. Dixon
Ultrasound of splenic variants, by A L. Hine and S R Wilson
A new method of changing occluded biliary endoprostheses, by A. Adam
An assessment of biopsy needles for ultrasound-guided prostatic biopsy, by S. Carter, A. Doble, N. O'Donoghue and J Wickham
Patterns of osteoarthritis in 100 geriatric patients, by C. W. Hutton, E. Wilkins, P. Maddison, P A. Dieppe and G Evison
Bone scintigraphy in osteoarthritis of the knee, by F C. McCrae, J. C. Shouls, M. Palmer, I Watt and P. A. Dieppe
Radiological types of Caisson disease and microbubble formation, by M. C Beverly and J. J Pflug

### IMAGE QUALITY OF ABDOMINAL COMPUTED TOMOGRAPHY IN THE ELDERLY

J. Baldwin, P. Sharpe, S. Cole and A. K. Dixon

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The hard-copy images of 96 randomly selected patients, age range 45–84 years, who underwent abdominal computed tomography (CT) were assessed to determine whether image quality is affected by age The total of 96 patients was made up of four male and four female groups. Each group of 12 patients varied in age (45–54 years, 55–64 years, 65–74 years and 75–84 years). In each patient the quality of the images was subjectively assessed by three independent observers. Wilcoxon's rank sum test was used to assess differences between the scores amongst the various groups and to check for any interobserver variation.

Contrary to what might be expected, there was only a slight reduction in scores with increasing age, and the difference in mean scores, even between the oldest and youngest groups, did not reach statistical significance. When the scores for men and women were separated, it was evident that the scores for the younger men (aged 45–54 years) were significantly ($p < 0.05$) higher than those for men aged 55–84 years. There was no statistically significant variation in scores among the female groups although some of the lowest scores were found in the youngest women There was only a statistically significant difference in the scores between men and women of similar age in the youngest group. These findings suggest that acceptable image quality can be achieved when performing abdominal CT in many elderly patients and that advanced age, by itself, should not be cited as a contraindication. Judging by the wide variation of the scores within each group, image quality depends more on the physical attributes and general condition of each individual patient.

### ULTRASOUND OF SPLENIC VARIANTS

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We report four cases in which unusual left upper quadrant abdominal masses were found on ultrasound (US) examination and subsequently proven to be splenic variants In two patients a round discrete mass was seen in the left suprarenal area, separate from a normal appearing spleen. A third patient had multiple masses in the splenic region and a fourth, post-splenectomy patient had a left posterior, para-aortic mass at the level of the renal hilum, which appeared most suggestive of lymphadenopathy. Computed tomography (CT) scans were performed in three cases and confirmed the US findings of a mass, but were not diagnostic of splenic origin. In two cases, the identified mass was biopsied, either percutaneously or surgically Confirmatory nuclear medicine liver/spleen scans were performed in three patients Single-photon emission computed tomography (SPECT) proved to be the most specific technique by demonstrating functioning splenic tissue in the region of the masses. Knowledge of the normal anatomy and embryology of the spleen readily explains the findings in our cases The polysplenic phylogenesis of the spleen may result in persistence of deep notches, occasionally giving the appearance of a mass of splenic tissue separate from the bulk of the spleen Accessory splenic tissue either at the splenic hilum or distant from the spleen may occur as a result of excessive primary splenogenesis. The possibility of splenic variants should be considered in the differential diagnosis of problematic, left upper quadrant masses seen on sonography

## A NEW METHOD OF CHANGING OCCLUDED BILIARY ENDOPROSTHESES

A. Adam

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The conventional method of changing occluded biliary endoprostheses involves percutaneous biliary drainage and the attempted manipulation of a catheter or guide wire into the endoprosthesis, followed by the introduction of an angioplasty balloon catheter to provide traction and effect removal of the stent. This method may fail either because of unfavourable biliary anatomy, which is often distorted by progression of the disease, preventing access to the occluded stent, or because of solid debris within the stent preventing the entry of the guide wire or catheter The alternative method of endoscopic removal and changing of an occluded endoprosthesis may be difficult if the stent does not project into the duodenum and it entails the risks of a papillotomy There is also the disadvantage that the insertion of a large-calibre stent in an ideal position within the liver of a patient with an advanced hilar cholangiocarcinoma is not easily achieved by most endoscopists

A new, relatively simple, rapid and effective method of changing occluded biliary endoprostheses is described the stent is cannulated with a 22-gauge Chiba needle under biplane fluoroscopic guidance prior to the injection of contrast medium Alternate injection and withdrawal of contrast medium through the needle clears the proximal end of the stent The 0.018 in guide wire of a modified Cope introduction set is then inserted into the stent, followed by the 6.3 French dilator and its metal stiffening cannula The 0.018 in wire and stiffening cannula are then withdrawn and a straight 0.038 in guide wire is introduced down the length of the stent. This provides a direct route to the occluded endoprosthesis and allows the easy introduction of a balloon catheter into it If the stent is too small for a balloon catheter to enter it, it may simply be pushed into the duodenum rather than withdrawn A new stent is then easily introduced through the stricture.

## AN ASSESSMENT OF BIOPSY NEEDLES FOR ULTRASOUND-GUIDED PROSTATIC BIOPSY

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A wide variety of devices for prostatic biopsy are available It is generally agreed that an adequate biopsy of ultrasonically defined prostatic lesions should include a core biopsy for histology and an aspiration specimen for cytological examination The method of action of prostatic biopsy needles falls into three categories· cutting a core, aspirating either a core or small fragments; the Menghini principle. Some of these devices are operated by hand, others by an automatic spring action or a purpose-built syringe, enabling easy one-handed action Each of the commercially available needles has been assessed using cadaveric prostates Cores are only reliably obtained by the cutting devices (Biopty and Trucut) and the Menghini method (Surecut) Paradoxically, larger needles do not necessarily produce better specimens The cytological specimens are best obtained by a purpose-designed needle with a serrated tip or a proximal side hole (Lee-Ray needle Cook urological) Many current machines for ultrasound of the prostate produce an axial image and the needle is identified in cross-section. A variety of experimental needles of various sizes have been investigated to establish the best tip configuration for accurate ultrasonic localisation. The effect of sandblasting the needles has also been examined There is little difficulty in identifying any needle, but the image obtained is best from bevelled needles with sandblasting. The size of the needle makes little difference to the imaging.

## PATTERNS OF OSTEOARTHRITIS IN 100 GERIATRIC PATIENTS

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Osteoarthritis (OA) may be a generalised joint disorder. Its occurrence in different joint groups would then be interdependent rather than a chance association. To test the hypothesis that there is dependence of joint involvement in OA at different sites, the patterns of OA in the radiographs of hands, knees and hips of 100 consecutive geriatric admissions were studied (mean age, 78 years, 28 men, 72 women). Each radiograph was read blind to patient identity and other radiographs Each joint was scored on a 0–3 scale with Grade 1 defined as joint space narrowing with subchondral bone sclerosis or osteophyte development. The occurrence of OA at each joint group (distal interphalangeal joints (DIP), first carpometacarpal joint and scaphoid trapezoid joint (first CMC), patellofemoral joint (PF), tibiofemoral joint (TF), and hips was analysed and $\chi^2$-test used to assess dependence between different joint sites The frequency of Grade 1 or greater joint involvement was 58% at first CMC, 41% at DIP, 49% at PF, 37% at TF and 23% at the hips. Only 13% had no OA at any site studied and only one had involvement at all joint groups There was significant association ($p > 0.01$) between the first CMC, hips, PF and DIP, but not the TF. There was also an association ($p > 0.01$) between the DIP and TF but not the hips or PF. These findings suggest OA is a generalised disorder with at least two patterns of joint involvement

## BONE SCINTIGRAPHY IN OSTEOARTHRITIS OF THE KNEE

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Bone scintigraphy is not a routine investigation of arthritis. Radiographs are currently used as a "gold standard" in evaluation of joint damage. It is, however, accepted that scan abnormalities can predate significant radiographic changes, reflecting early disease activity. Moreover, previous work from this unit looking at hand osteoarthritis (OA) has shown that the scan may be normal in spite of obvious radiographic damage Less deterioration after 5 years was seen in the joints of those who had normal as opposed to abnormal scans. Scintigraphy is being further evaluated in the knees of 130 patients with OA. Scans obtained using $^{99}$Tc$^{m}$-HMDP and standard Weight-bearing radiographs of the knee were analysed separately by a single observer. Our results indicate that a significant number of joints showed discrepancy between radiography and scintigraphy Not only did normal activity occur with normal radiographs, but also the converse was seen This discrepancy varied between compartments of the knee, being most marked in the lateral and patellofemoral joint. Several different scintigraphic patterns have emerged These include diffuse uptake around the whole joint, responsive to intra-articular steroids (synovial?); discrete uptake around the joint margin only (active osteophyte formation?); diffuse subchondral bone uptake; and the "hot patella" which may be an isolated feature of otherwise normal knees. Correlations between all clinical, radiographic and scintigraphic features are being analysed. Scintigraphy adds a new dimension to the standard clinical and radiographic assessment of OA of the knee. It may help to distinguish subsets and provide prognostic information and insights into the different aspects of the disease process.

## RADIOLOGICAL TYPES OF CAISSON DISEASE AND MICROBUBBLE FORMATION

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A double mechanism for caisson disease is postulated. Intraosseous pressure was measured in 10 volunteers during slow walking and was found to fluctuate by up to 100 mm Hg (Beverly et al, 1987). Heparinised whole blood was decompressed in a chamber while being scanned ultrasonically to detect bubbles 10–100 $\mu$m in diameter. A computer recorded the numbers of bubbles present (Gallagher & Pearson, 1973). Lowering the pressure resulted in the appearance of showers of microbubbles, which persisted during the maintenance of negative pressure. At atmospheric pressure the bubbles cleared slowly (30 min) By applying increased pressure to the chamber the bubbles redissolved more rapidly (10 min) Curves showing the effect of saturation with air, nitrogen, oxygen, carbon dioxide and helium were produced. Microbubbles are formed within blood during acute decompression These extra-osseously formed bubbles are selectively trapped in the relatively non-distensible matrix of cancellous bone and some tough neurological tissues. Softer organs pass the micro-bubbles Cyclical physical loading of bone, such as that experienced during walking, causes fluctuating intraosseous pressures. The brief negative phases encourage further intraosseous microbubble formation within the weight-bearing cancellous bone. The "weightless" diver thus experiences a generalised pattern of caisson disease whereas the weight-bearing tunneller has 12 times the incidence of radiological necrosis of the femoral head (Decompression Sickness Central Registry, 1981).

This work was supported by a grant from the Wellcome Trust

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# Posters. Clinical: Gastrointestinal Tract and General

**Chairman: Dr F. J. Brunton**

Ultrasound of the gut, by A M. K. Thomas and I. Shirley
Transient diverticula of the colon, by J. Rawlinson and F J Brunton
The aetiology of angiodysplasia: a new concept, by A. P. Hemingway
Defecography· a study of normal volunteers, by P. J Shorvon, S. McHugh, G W Stevenson
Defecography a necessary examination in the diagnosis of constipation, by E Mangel, H Schmelzer, B Eibl-Eibesfeld, St Muller-Lissner, L Sepp-Lukas, K J Pfeifer
Diagnostic imaging of carcinoid tumours with specific iodine-131 meta-iodo-benzylguanidine scintiscanning and computed tomography, by J Adolph, B. Kimmig and P Georgi
Continuing defect in cerebral energy metabolism in patients with persistent hepatic encephalopathy· monitoring with phosphorus-31 magnetic resonance spectroscopy, by B. D Ross, M Y Morgan, I. J Cox, K. E Hawley and I R. Young
Energy metabolism of normal and pathological liver in man demonstrated by phosphorus-31 magnetic resonance spectroscopy, by B. D. Ross, D R Bailes, D J Bryant, G M Bydder, H. A Case, I J. Cox, H Hodgson, M. Morgan, D. Robinson and I R Young

## ULTRASOUND OF THE GUT

A. M. K Thomas and I. Shirley

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The use of ultrasound is usually of limited value in the study of gut pathology, in part because of the presence of intestinal gas In a number of cases, we have found ultrasound to be of value and to have provided information when other imaging modalities have been inappropriate. Areas of use include: bowel wall thickening due to malignancy, lymphoma, inflammatory disease and hypertrophic pyloric stenosis; bowel obstruction, including gastric outlet obstruction and fluid-filled small-bowel obstruction, and congenital lesions, including the intra-uterine detection of anterior abdominal wall defects and small-bowel atresias and volvulus Visceral situs can be determined post-natally Illustrative examples are presented

## TRANSIENT DIVERTICULA OF THE COLON

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Transient colonic diverticula are a phenomenon that can be observed radiologically in a minority of patients undergoing a barium study of the large bowel Radiographs before and after the administration of a smooth-muscle relaxant (Buscopan, Boehringer Ingelheim Ltd, 20 mg) are taken Diverticula seen on the early radiographs can, in some patients, disappear after colonic muscle relaxation Using this technique in 441 consecutive barium enemas performed during the period 1985–86, transient diverticula were observed in 18 patients (4 1%) Transient diverticula were seen predominantly in the left hemicolon and mainly in the older age group (mean age 64.5 years). They were associated with sigmoid diverticular disease in six patients and with pre-diverticular spasm in four patients These observations suggest that transient diverticula represent an early stage of the disease. The response to smooth-muscle relaxants confirms the important role of the colonic muscle in the pathogenesis of diverticula

## THE AETIOLOGY OF ANGIODYSPLASIA: A NEW CONCEPT

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Angiodysplasia is the term used to describe microvascular abnormalities found in the mucosa and submucosa of the wall of the large intestine involving predominantly the caecum and ascending colon These abnormalities cannot be detected on barium examination or at laparotomy They are most commonly diagnosed at either angiography or colonoscopy Angiodysplasia is regarded as being one of the commonest causes of obscure gastrointestinal bleeding, particularly in the elderly patient. Treatment may be supportive or entail either endoscopic coagulation or surgical resection, depending on the extent of the disease. In resected specimens it is difficult for the pathologist to localise the abnormality without the aid of special injection techniques

Several theories relating to the aetiology of angiodysplasia have been proposed. The most widely accepted is that it is a degenerative condition related to aging and chronic ischaemia, giving rise to microvascular mucosal arteriovenous shunts. Our experience suggests that this is not necessarily the entire answer. We have diagnosed the condition in a number of patients under the age of 30 years, and have also found it in association with another congenital abnormality, namely Meckel's diverticulum Over the last 7 years we have diagnosed the condition in over 70 patients, at least half of whom have undergone resection of the affected segment of bowel In those specimens that we were able to examine with special injection techniques it has become apparent that the lesions are always clustered opposite the ileocaecal valve and that they become less frequent the farther away from the valve one looks. We wish to postulate that angiodysplasia has a multifactorial aetiology, at least one factor being the chemical effect exerted on the mucosa of the caecum by the small-bowel contents. As not everyone is affected by this condition it also seems likely that some people have a congenital predisposition to its development.

## DEFECOGRAPHY: A STUDY OF NORMAL VOLUNTEERS

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There is increasing interest in the use of defecography for investigating ano-rectal disorders, but all previous studies suffer from the absence of data on normal subjects. Forty-eight healthy young adult volunteers (25 men and 23 women) were recruited from the student population of Toronto to undergo a defecogram. "Normality" was tested by an extensive questionnaire on personality traits, cognitive function and bowel habit For the procedure a barium paste was inserted into the rectum after initial coating of the rectal mucosa with liquid barium The external anal orifice was marked with barium ointment, and the women inserted a tampon soaked with contrast agent into the vagina. The subjects were screened in the lateral position and video recordings with 100 mm spot films were taken at rest, with contraction of perineal and anal muscles, on straining and finally during defecation. Twenty variables were measured directly from the 100 mm films using a centimetre midline scale incorporated in the system. Ten radiographic appearances were also recorded and graded where appropriate. From these measurements it became clear that the range of normality was much wider than previously realised 44% of the men and 45% of the women had a high-grade intusussception, 77% of the women had some degree of anterior rectocele, which was graded as moderate to large in nine (39%). The mean pelvic descent during defecation in women was 2.0 cm (SD 1.5 cm) and was greater than 3 cm from the rest position in 23%. In men the mean descent was 1.9 cm (SD 0.97 cm), with 20% greater than 3 cm Four subjects (three women, one man) had an open anal canal at rest with apparent incontinence. These findings indicate that defecograms must be interpreted with more caution than in the past.

## DEFECOGRAPHY: A NECESSARY EXAMINATION IN THE DIAGNOSIS OF CONSTIPATION

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Chronic constipation is a very common disorder. Until now the diagnosis has been unsatisfactory and therefore therapy is mostly inadequate. By defecography we tried to examine not only the morphological but also the functional aspect of defecation disorders. We performed these examinations in 80 patients The rectum was filled with a soft, stool-like contrast medium. A film sequence (1 frame/s) during defecation was taken with the 100 mm camera in lateral images while the patient was sitting on a camping toilet. We found several ano-rectal disorders. descent of the pelvic floor with abnormal ano-rectal angle, prolapse of the mucosa, intussusception of the rectum, and rectocele. All patients were treated successfully, mostly by surgery

## DIAGNOSTIC IMAGING OF CARCINOID TUMOURS WITH SPECIFIC IODINE-131 META-IODO-BENZYLGUANIDINE SCINTISCANNING AND COMPUTED TOMOGRAPHY

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The radiological diagnosis of carcinoid tumours has remained a problem because of unspecific findings. In order to assess the value of $^{131}$I meta-iodo-benzylguanidine (MIBG) scintiscanning and computed tomography (CT) in carcinoid tumours of various origin, we have investigated nine patients with histologically proven carcinoids , located in the gastrointestinal tract (four patients), bronchus system (three patients) and thymus (two patients). Metastatic deposits were present in five patients, involving mesenteric lymph nodes, lung, liver, spleen, bone, peritoneum, and cerebrum. Computed tomography clearly depicted the tumours and metastases in relation to surrounding vital structures (*e g.* great vessels and spinal cord) The CT finding of an abdominal soft-tissue mass with a radiating pattern of linear densities in the mesenteric fat was found to be highly suggestive of intestinal carcinoids Characteristic CT features could not be determined for carcinoid tumours in bronchus or thymus or for liver metastases from carcinoids. Iodine-131 MIBG scintiscanning yielded positive results in five patients whose tumours and metastases exhibited intense persistent uptake The overall sensitivity of MIBG scintigraphy was 76%, with values of 100% in intestinal carcinoids and 67% in bronchus carcinoids No MIBG uptake was observed in carcinoids in the thymus. With regard to a few other concentrating tumours of neuroectodermal origin which can be easily differentiated from carcinoids, MIBG scintiscanning is considered the first imaging modality to be really specific for carcinoid tumours We conclude that $^{131}$I MIBG has diagnostic and therapeutic potential in carcinoids, especially of intestinal origin.

## CONTINUING DEFECT IN CEREBRAL ENERGY METABOLISM IN PATIENTS WITH PERSISTENT HEPATIC ENCEPHALOPATHY: MONITORING WITH PHOSPHORUS-31 MAGNETIC RESONANCE SPECTROSCOPY

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Cerebral energy metabolism is thought to be impaired in patients with persistent hepatic encephalopathy (PHE); oxygen consumption and glucose uptake across the cerebral circulation are reduced. Treatment results in improved cerebral oxygen consumption but blood flow may remain lower than normal A standard test of cerebral metabolic function has been developed, using $^{31}$P magnetic resonance spectroscopy (MRS), to determine cerebral high-energy phosphates (adenosine triphosphate (ATP) and phosphocreatine (PCr)) levels and inorganic phosphates (Pi) (Pi/PCr and Pi/ATP) levels and intracerebral pH in a constant volume of the forebrain Eight patients with proven PHE and eight control subjects were examined In the patients, cerebral blood flow, oxygen consumption, glucose uptake and blood bicarbonate, phosphate and standard liver function tests were performed. All patients were examined with MRS while receiving their normal treatment. Relative concentrations of metabolites in the spectra were determined from peak areas, and pH from the chemical shift of Pi.

A significant reduction in intracerebral Pi level was observed in PHE subjects (Pi/ATP = 0.29 ± 0.03; Pi/PCr ± 0.17 ± 0.01 versus Pi/ATP = 0.46 ± 0.06; Pi/PCr = 0.27 ± 0.03· $n = 8$, $p < 0.01$ (Student's *t*-test)). Plasma Pi level was identical in the two groups Intracerebral pH was unaltered (7.10 ± 0.06 versus 7.05 ± 0.04 in controls) The ratio PCr/ATP was unchanged. Patients were ranked on the basis of psychometric tests and cerebral blood flow, which correlated broadly with the cerebral Pi level, determined by $^{31}$P MRS. We conclude that $^{31}$P MRS demonstrates a defect in cerebral energy metabolism in PHE, and suggest that the previously noted reduction in cerebral oxygen consumption may be the direct result of reduction in intracerebral Pi content

### ENERGY METABOLISM OF NORMAL AND PATHOLOGICAL LIVER IN MAN DEMONSTRATED BY PHOSPHORUS-31 MAGNETIC RESONANCE SPECTROSCOPY

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We have studied the potential role of localised $^{31}$P magnetic resonance spectroscopy (MRS) in monitoring liver metabolism in a group of patients and volunteers. The spectral resolution achieved is very good, enabling a more detailed assessment of the metabolic status of the liver than hitherto. Spectra were obtained using a Picker 1.6 T research spectroscopy system. Phosphorus-31 spectra were obtained both from the whole sensitive volume of the 6 cm diameter receive coil and from 1 cm slices parallel to the plane of the receiver coil using a one-dimensional phase encoding technique. Using the latter method, spectra typical of liver can be readily obtained without contamination from surface muscle. The spectrum of normal liver is dominated by six resonances: phosphomonoester (PME), phosphodiester (PDE), inorganic phosphate (Pi) and three from adenosine triphosphate (ATP). Examples of metabolite concentrations are $[\mathrm{PME}]/[\mathrm{Pi}] = 0.2 \pm 0.05$, $[\mathrm{Pi}]/[\beta\mathrm{ATP}] = 0.5 \pm 0.1$. The J-couplings of the ATP resonances were generally observable. Further, individual contributions to the PME and PDE peaks could be distinguished and resonances assigned to pyridine nucleotides. The effect of fasting and exercise on the normal liver spectrum was studied. A range of diffuse hepatic pathologies was studied, including cirrhosis, metastatic disease and hepatic venous occlusion. In several cases the spectral changes were only subtly different from normal liver tissue. The concentration of PME was not found to be diagnostic of cirrhosis. Some patients, however, demonstrated dramatic changes, such as a fivefold increase in $[\mathrm{PME}]/[\beta\mathrm{ATP}]$ ratio in a patient with Budd–Chiari syndrome. The relationship between these findings and individual pathologies is discussed. Despite the speculative nature of the underlying biochemical changes, we conclude that localised $^{31}$P MRS can be used to monitor metabolism in both health and disease.

BIR Bulletin

August 1987

# Radiology '87

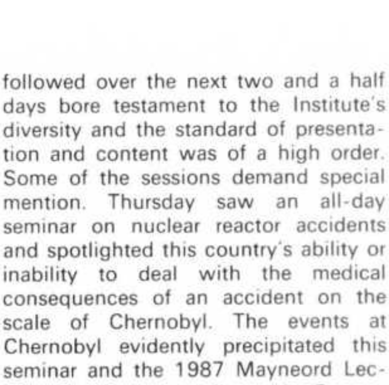
## A personal view

By Dr David Rickards

Like its two predecessors, the annual congress of the British Institute of Radiology, Radiology '87, was held in a city with strong maritime connections. Bristol in '86 and Manchester in '85 because the president at the time lived and worked there or thereabouts, Southampton in '87 because this year's president spends some of his spare time embarking on the underwater nuclear fleet of Her Majesty's Navy to locations of the utmost secrecy. Even the secretariat of the BIR, that most persistent and efficient band of people, are unable to communicate with him during these subaquatic voyages, but Southampton '87 found him at his most approachable, available and presidential best. Like Gerald Hoffnung, who discovered that he was actually born when he was 2, Southampton '87 started the day before April Fools' Day with the congress committee and the BIR staff descending upon the Boldrewood centre to establish a beachhead from which the rest of the congress would run smoothly and efficiently. Their daytime efforts to this end were rewarded with an evening reception which the congress organisers shared with early registrants to the congress and with those who got it wrong and found themselves in Southampton a few hours early with nothing better to do! I'm also informed that a sneak preview of the technical exhibition was permitted to avoid the rush expected in the following three days! What is certain is that by that time all the hard work in preparing for the congress was now on autopilot. By Tuesday evening, the RAC had erected fool-proof signs for those entering the city from whatever direction, except a seaborne approach, congress buses were primed, the technical exhibition in place, vegetarian dishes for those inclined ordered and a rain-free three days prayed for, just for the convenience of those attending.

It is sensible to start a congress officially at mid-morning. It permitted many people the opportunity to travel that morning, thus saving an extra night's expense in a hotel for those attending from first to last paper. It also precipitated the BIR grand prix down the M3 during which the speed limit was universally ignored and no winner declared. At 9.30 on Wednesday morning, the president officially opened the congress and commenced a tour of the exhibits that formed the technical exhibition, and at 11.30 delivered his presidential address. Roger Berry started by stating that he knew what he had to do, knew what he wanted to do, but wondered how to make it interesting. On the subject of "The Institute at 90", he animatedly and with obvious great enjoyment described the Institute's origins which, somewhat surprisingly, were in that bastion of another profession, 5, Pump Court in the Inner Temple. On this building is a sundial suitably inscribed with the legend "shadows we are and like shadows we depart". The Röntgen Society did depart the law courts and now has its own splendid home in Portland Place. He tabulated the events of the intervening 90 years, culminating in the formation of the present multidisciplinary institute, and ended by stating that the Institute's strength was its diversity and its future in the gift of its members' enthusiasm.

The academic programme which followed over the next two and a half days bore testament to the Institute's diversity and the standard of presentation and content was of a high order. Some of the sessions demand special mention. Thursday saw an all-day seminar on nuclear reactor accidents and spotlighted this country's ability or inability to deal with the medical consequences of an accident on the scale of Chernobyl. The events at Chernobyl evidently precipitated this seminar and the 1987 Mayneord Lecture that afternoon delivered by Frances Fry detailed the effects of Chernobyl on the UK. It was an excellent session, enhanced by two speakers from Russia. Following Chernobyl, the Russians rather uncharacteristically bared their souls in Vienna and produced for the Western scientific fraternity a detailed account of what went wrong in



Professor Roger Berry with radiographer Mrs Val Berry.

FOTHERGILL COMPOSITE & POLYMER TECHNOLOGIES LTD

*The president meets the exhibitors.*

*Dr John Stock of Manchester arranging his slides in the Kodak audio-visual service centre.*

Chernobyl, how they had cared for the injured and those at risk and what they intend to do about preventing further catastrophes. Following Vienna, the Russians seem to retreat into their shells and little was heard of the sequelae of the nuclear accident. The appearance of the two speakers from Russia in Southampton perhaps signals a further flow of information between Russian and Western scientists and they were made very welcome by the delegates who attended the seminar.

On Friday there was an all-day seminar on therapeutic ultrasound. To the vast majority of diagnostic radiologists, I suspect the concept of ultrasound being anything other than diagnostic to be an anathema and to warrant very little time in the academic agenda. The session was reasonably well attended and proved that the therapeutic aspects are potentially legion and have already dramatically altered the treatment of some conditions. Will ultrasound leave the realms of non-intervention on the strength of its therapeutic ability? Therapeutic radiologists are interventional. A new breed of interventional ultrasonologists is to be expected!

Sir John Batten delivered the Royal College of Radiologists' George Simon Lecture. Appropriate for one of the country's leading chest physicians honouring the name of the grand old man of chest radiology. The Mackenzie Davidson Memorial Lecture was given by Professor M. J. Peckham on the subject of the clinical biology of testicular germ-cell tumours. An innovation to the BIR congress this year

*President Roger Berry with the BIR Programme Team, led by Mrs Shirley Gaffey (second from right) with Sue Turner, Sarah Tasker and Penny Reeves.*

*Industry Committee member John Twydle with BIR honorary secretary Mrs Jean Harvey.*

was poster sessions. Each day a series of posters was available to be viewed by delegates and that afternoon in the semi-lunar intimacy of the Padua theatre the posters were quickly reviewed by the chairman of the session followed by a discussion of each poster with an author. Seven or eight posters per session were dealt with in a half-hour period. It would seem that poster sessions are a good idea, allowing many presentations in a short time in the relaxed and informal setting of a small theatre. The success of a poster session largely depends on the chairman's ability to promote discussion with a fairly jaundiced eye on the time taken! The quality of the posters produced was excellent and all presenters are to be thanked. As an innovative move, the poster sessions can be deemed a success and should form a permanent part of the Institute's annual congress.

The technical exhibition covered the best part of two floors and was located in juxtaposition to all the lecture theatres, restaurants and the bar, which, rather surprisingly, was small and boasted no seating and was in fact part of a self-service cafeteria. I gained the impression that the exhibitors were a lot happier with the arrangements made for them this year. It is important that they should be close to where the delegates spend their time so that they may have maximum impact. The financial success of the congress is in part dependent upon our commercial colleagues. The exhibits were colourful and professionally presented. No CT scanners this year, but perhaps the weight restrictions of the floors didn't permit the showing

*Left to right: Professor Berry, Miss Frances Fry, Mayneord Lecturer, who spoke on the impact of the Chernobyl reactor accident on the UK, Mr B. Goldthorpe of 3M (the sponsors) and Professor Mayneord.*

*Congress Committee:*
Professor R. J. Berry (Chairman)
D. V. B. Batty
Dr M. Gowland (Scientific Exhibition)
Mrs M. J. Harvey (Publications/Publicity)
Professor C. R. Hill
Dr R. D. James
Mr G. Mountford (Technical Exhibition)
Dr P. H. S. Smith (Scientific Programme Chairman)
Professor P. N. T. Wells
Professor B. S. Worthington
Miss S. Johnstone (General Secretary BIR)
Mrs S. Gaffey (Assistant Secretary: Programme)

*Professor Berry with the Mackenzie Davidson Memorial Lecturer, Professor M. J. Peckham.*

*Speeches by... Professor Berry, Lady Anglesey and Professor Rhys Davies, President of the RCR.*

*The prime movers: (left to right) Grahame Mountford, director of the technical exhibition (with wife Jenny), President Roger Berry, and Peter Smith, chairman of the scientific programme, with wife Anne.*

of heavy radiological equipment. The annual dinner at the Polygon hotel was memorable for the quality and inherent humour of the speeches. It is reassuring to learn that the spirit of Stanley Holloway is alive and well in Portland Place The informal BIR golf session the following day was noted for the age-old golfer's problem of standing too close to the ball after he's hit it! One record was broken A well known central London ultrasonologist managed to 6 putt from 8 feet with total sincerity and complete lack of understanding of the rudiments of the game What he's going to do in Scotland next year defies the imagination.

There are many unsung heroes who make a congress go smoothly. The permanent staff of the BIR, so ably headed by Susan Johnstone, were instantly recognisable in their blue sweat-shirts. Registration formalities for the delegates were quick and painless and all problems were dealt with efficiently. Kodak deserves great praise presenters of papers were able to view their slides irrespective of the number of projectors used and, once in the right order, they were despatched to the correct lecture theatre to be returned to a central location after the session for collection I do not think any slips were made and Tony Oxley's professionalism is to be admired. Such a service makes the nerve-wracking task of presenting one's work all the easier.

The annual BIR congress in Southampton was a success and all those who helped organise it deserve great credit. It is the largest meeting of the British radiological calendar, this year attracting a total of 474 delegates, slightly down on last year Diagnostic radiologists accounted for 131 and more physicists attended than radiotherapists. It is more than likely that anyone reading this attended the meeting and so I may be preaching to the converted, but if British radiological meetings are to survive as an international forum for radiological debate and continuing education, such meetings as the BIR congress demand the support of those who work in the radiological field. On the whole, the BIR congress does not receive sufficient support, which is a tragedy. Glasgow hosts the '88 congress and I wish it every success and hope that it gets the support and active participation of many more who work in the ever-increasing and divergent field of radiology.

**British Institute of Radiology**
**46th Annual Congress**
*incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting and in collaboration with the Scottish Radiological Society*

## Radiology '88

Glasgow May 23–25, 1988

Glasgow will be the first in a series of back-to-back meetings with the Annual Conference of the College of Radiographers The technical exhibition will span both meetings and be the manufacturers' showcase in 1988.

The place: the brand new Scottish Exhibition and Conference Centre

Radiology '88 will cover all aspects of radiology: X-ray diagnosis, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines

Proffered papers and posters are invited: closing date November 30 1987

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# International Conference on Nuclear Containment

This event, held at Robinson College, University of Cambridge, April 6–8 this year, was successful in a number of ways. Perhaps the first point which comes to mind is the insight of the Conference Chairman, David Walton, who gathered together an active steering committee some months before the Chernobyl accident in April 1986. The low attendance (about 150) is somewhat surprising given the abundance of literature published since the accident The RBMK is a reactor design in which the barriers to the release of radioactivity to the public and the environment was, in hindsight, suspect. Nevertheless, all other nuclear utilities are now examining their own designs of containment and, indeed, all aspects of safety.

The conference brought together a range of experts on containment and the standard of technical papers was high. A total of 32 papers were read, in four sessions. containment structures, systems, transport handling and storage, and predictive analysis safety and regulatory approaches. In a short address of welcome in opening the conference, the President of the Institution, Mr Keith Simm, made mention of Chernobyl and its minimal design of barriers of containment before introducing the first of the four session chairmen, Mr John Derrington, former Director of Sir Robert McAlpine & Sons Ltd.

In the session on containment structures, Gary Zakaib of Ontario Hydro showed his organisation's practice and performance in ensuring the highest standards of containment by discussing a specific testing programme. To the delight of the large number of delegates who remained in the lecture theatre at the end of the afternoon, he presented an exciting video taken during some LOCA tests for checking effectiveness in minimising releases to the environment The question of primary containment at Sizewell B was amongst those papers on structures and systems on the first day Ian Todd of the NII spoke on the regulatory approach to the assessment of containment with reference to the Sizewell B design. Other papers addressed modelling, with specific reference to a much used one-sixth model constructed for concrete-containment testing at the Sandia National Laboratories, New Mexico. A paper by J K Joosten of the International Atomic Energy Agency about the Soviet RBMK-1000 containment system aroused a great deal of interest. He described the reactor's philosophy of containment, both primary and secondary, and stressed that the design is not unique, as has so often been quoted, but does have variations in concepts utilised by other reactor types He claimed that the containment failure mechanisms at Chernobyl are relevant to the entire industry and must stimulate a general re-examination of containment philosophy Questions on whether "single failure" criteria are sufficiently bounding and whether present designs take account of the independence of various components need to be urgently addressed Maybe a higher standard of safety should be pursued by building a third barrier Dr Mike Hayns, Head of Safety & Reliability Directorate, wound up the conference with a paper entitled "The changing role of LWR containment in nuclear safety". Dr Hayns spoke as chairman of a working group on nuclear safety of the Nuclear Energy Agency of the Organisation for Economic Co-operation and Development.

Excellent audio and visual effects are afforded by Robinson College. The conference was accompanied by an exhibition, but unfortunately the college does not lend itself to such events.

The poster sessions were an undoubted success. However, in some cases there was an extremely thin line to be drawn between the poster work and that appearing at the exhibition stands. Perhaps a stricter control in this area is needed.

Sir Alan Cottrell, formerly Master of Jesus College, Cambridge and Board Member of the UK Atomic Energy Authority, was the guest speaker at the conference dinner. He spoke in a light-hearted, but by no means flippant manner, covering a number of matters of interest to us all.

Overall, the conference further enhanced the good name of the Institution, not only by those delegates who attended, but also by the members of the large engineering concerns directly involved. Members of the Institution who have never attended one of its conferences before should make every effort to come to the next one.

F. John L. Bindon

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# Obituary

## William J. Stripp, M.B.E.

Bill Stripp died on April 8, 1987, at the age of 69 years. He came from a military family, travelling extensively as a child and being educated at the Lawrence Royal School in India.

In 1939, just before the outbreak of war, he trained as a radiographer in the RAMC, being based at Millbank. He subsequently served with the British Expeditionary Force in France, being one of the last to be evacuated from Dunkirk. He later served as a radiographer in Freetown and Lagos. Later in the war, he became at one time Ben Felson's radiographer at Netley and the two remained firm friends. On his return to civilian life, he spent three years in X-ray engineering, becoming a member of the Society of X-Ray Technology; he retained this technical interest throughout his long and distinguished career in radiography.

He passed the membership examination of the Society of Radiographers in 1946, being appointed as Superintendent Radiographer at the Royal National Orthopaedic Hospital (RNOH) in Great Portland Street in 1950. It was from this post, until his retirement in 1983, that he exerted his major influence on the practice of orthopaedic radiography. In his practice and the publications of his early career, he was the epitome of the specialist "working" superintendent radiographer, a relatively novel concept. His innovative approach and practical teaching ability came to the attention of Miss Marion Frank who amongst others, persuaded him to widen his teaching sphere by lecturing to various schools of radiography. Soon afterwards followed the practice of secondment of students from the various radiographic schools in London to the RNOH for practical instruction in orthopaedic radiography; this arrangement continues to this day at both the town and the country branches of the RNOH. His increasing reputation led to his invitation to undertake lecture tours in the United States and Australasia. In the United Kingdom also, his ability as a teacher was recognised. He was well known to successive generations of radiologists and orthopaedic surgeons, to whom he was able to show the precise demonstration of anatomy by radiographic means, without the restriction of standard projections alone. He was awarded the Honorary Fellowship of the College of Radiographers for services to the profession.

Many of his innovative techniques were not published, but at the instigation of Dr Ronald Murray and Professor Harold Jacobson he was encouraged to write a section on special techniques in orthopaedic radiography in *The Radiology of Skeletal Disorders;* published also as a separate book, this remains an invaluable specialist text for radiographers and radiologists today.

His contribution to his profession was recognised when in 1983, in the year of his retirement, he was awarded the MBE in the Birthday Honours List.

Bill Stripp was highly respected, not only because of his outstanding professional ability, but for his unvarying cheerful disposition, his humility and his caring attitude towards patients and students alike. His attitude to his radiographers was good humoured and paternal; he frequently was to be seen escorting them to the underground station at the end of a working day, to ensure their safe conduct on a dark night. The inflexibility of the Whitley scales made him pay heavily for his dedication to running a small specialist department, but he rarely complained. His concept of quality control was the personal checking of every film taken during the day.

He could quickly spot a "good practical radiographer" and was rarely if ever wrong. During his period as Superintendent Radiographer, it is doubtful whether the need to advertise the position of replacement radiographer ever arose; he always knew of a suitable replacement. His relationship with the orthopaedic consultants was such that they rightly depended upon his expertise to solve their problems by appropriate radiographic methods. This sometimes led to the problem of which special "Stripp" view was being requested in a particular case!

His main outside interest lay in his family and in his enchantment with trains both model and real.

With his passing an era has also ended; he possessed a unique character and restrictions in present day practice make it unlikely that anyone with his combination of technical expertise and grass-roots wisdom will ever again emerge.

Above all, by his untimely death, we all have lost a friend and colleague whose warmth and comradeship spread far beyond the hospital that he loved.

He is survived by his wife Joan, his daughter Ann, sons Alan and David and his grandchildren, in whom he delighted. He will be greatly missed.

Dennis Stoker

# Press releases

### Measures to deal with radon in dwellings: NRPB advice

Advice to the government to limit radiation doses in dwellings from the naturally occurring radioactive gas radon has been published by the National Radiological Protection Board (NRPB) in *Exposure to Radon Daughters in Dwellings. ASP10*. The document includes recommendations on action to be taken in some existing dwellings and measures to limit doses in future dwellings.

Over the past few years, NRPB staff have measured radon in approximately 3000 dwellings throughout the UK, in detail in those areas where high concentrations would be expected to occur. The average radon concentration indoors is around 20 Bq m$^{-3}$, but some values above 1000 Bq m$^{-3}$ have been discovered in southwest England. In terms of effective dose equivalent, these correspond to an annual average of around 1 mSv, with some values exceeding 50 mSv.

Exposure to radon daughters may cause lung cancer. There is no direct evidence that this occurs in the home, but the risk may be estimated from studies of miners who were exposed at work. The lifetime risk of lung cancer from lifetime exposure to radon daughters in dwellings is estimated to be about 2% at an action level of 20 mSv per year. The average risk of lung cancer in the UK from all causes is about 6%.

The Board took account of relative risk, feasibility, cost and numbers of dwellings involved when developing its recommendations, which are expressed as follows in *ASP 10*:

> "For *existing dwellings*, graduated measures related to effective dose equivalent are recommended above an Action Level of 20 millisieverts per annum. At this Action Level, simple action to reduce exposure to radon should be taken: at a level several times higher, severe action is likely to be necessary . . . the dwellings with the highest levels should be given priority.
>
> For *future dwellings*, an Upper Bound of 5 millisieverts per annum is recommended as the basis for implementing changes to building procedures in areas of the country where high levels of radon are likely."

The number of dwellings in which the annual dose may exceed 20 mSv per annum is about 20 000 and 50 mSv per annum about 2000. The number of new dwellings built each year in which 5 mSv per annum may be exceeded is a few thousand.

The Board will co-operate with the Department of the Environment and the Building Research Establishment in a programme of work to implement the recommendations. This will involve the identification of houses and areas where high concentrations of radon occur, and the development of methods to reduce and prevent such concentrations.

Further information and *ASP10* are available from: NRPB Information Office, Chilton, Didcot, Oxon OX11 0RQ.

### National Centre of Responsibility Newsletter

The first issue of *Focal Point*, the newsletter of the National Centre of Responsibility (CoR) for Diagnostic X-ray Equipment, Maintenance and Silver Recovery was published in March.

In 1982 the contracting and purchasing previously undertaken by the DHSS Supply Branch was devolved to the NHS regions. This resulted in the individual regions placing their own X-ray equipment orders and the Regional Supplies Department at South East Thames Regional Health Authority (RHA) taking responsibility for the organisation of the National Equipment Contract.

In 1984 the Health Service Supply Council proposed the establishment of national centres of responsibility for a wide range of commodity groups. Each would become a centre of expertise in its subject, acting as a link between the NHS and the industry in question. Based at South East Thames RHA in Bexhill, East Sussex, the national CoR for Diagnostic X-ray Equipment, Maintenance and Silver Recovery started operating in January 1985.

*Focal Point* will be of interest to everyone concerned with radiology in the NHS, and also to people in the X-ray manufacturing and supply industry. For more information, please contact: Paul Bryden, Press and Public Relations Officer (Tel. 0424-222 555 ext. 2156).

### Technegas generator

An instrument described by a past president of the US Society of Nuclear Medicine as "one of the most significant advances in lung function imaging in nuclear medicine in the last 10 years" was invented and developed and is now offered for sale by Tetley Technologies in conjunction with the ACT Health Commission.

The resolution of the technetium-99m label is superior to existing gases and allows computer superimposition and subtraction from the perfusion scan for pulmonary embolism. Because penetration of the "gas-like" particle is similar to that of true gases, dynamic rates of ventilation can be done and the images are free from central airway deposition. The image is persistent and is not cleared by further breathing or active transport. Unhurried and gated images are thus possible. For the first time it is possible to acquire single-photon emission computed tomography images of the lungs, and using the new GE surface reconstruction software it is possible to produce high-quality surface images of the lungs.

Even patients with compromised breathing or those on breathing support can have an effective ventilation study with Technegas. Elimination of room contamination of gases is also possible, with a fully effective filter and breathing of the Technegas on demand rather than under pressure.

### Radiation Measurements, Inc., introduces automatic exposure control and mammographic kVp digital meters

The Digital Automatic Exposure Control (AEC) Meter, Model 235, has been developed to provide the user with a convenient, fast, and accurate method of testing automatic exposure controls of X-ray units. The expense and inconvenience of doing these tests with film are avoided using the Model 235 AEC Meter. The Digital Mammographic kVp Meter, Model 232, provides a convenient, fast, and accurate method of measuring the kV of mammographic units. The Mammographic Meter reads kV ranges from 22 to 60 kVp with an accuracy of ±(1 kV + 2%).

For more information, please contact RMI, PO Box 327, Middleton, WI 53562, USA.

### BIR Ties

BIR ties are available to members at £5 each (£6 including post and packing). They are navy blue or maroon red and carry the rays from the Institute's logo, in gold. Please send a cheque payable to the BIR with the order.

# BIR calendar events

*Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085).*

*The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.*

**Imaging in Dementia**
October 15, 1987 at 5.30 p m
Organised by the Diagnostic Methods Committee Speakers: Prof. R. Levy, Dr R. Wise, Dr P. J. Ell, Dr N. Antoun and one other.

**Chemical Modification of Radiation Effects: Experimental and Clinical**
November 13, 1987
All-day radiobiology work-in-progress meeting.

**New Radiopharmaceuticals and Their Clinical Applications**
November 27, 1987
Scientific Societies, London W1
Organised by the Nuclear Medicine Subcommittee.
Speakers: Dr I Brown, Dr B Langstrom, Prof N A. Lassen, Dr H. J. Machulla, Dr A. D Nunn, Dr J. Thornback and Dr G. D. Zanelli

**Lasers—Applications In Radiology**
January 14, 1988 at 5.30 p.m.
Joint BIR/RCR/RSM meeting.
Chairman Dr W D. Jeans
Speakers. Dr A. L Mackenzie, Dr D. C Cumberland, Dr S G. Bown, Mr D Rothery, Dr G Watson and Dr S Hart.

**Institute Sponsored Visits**

Members should write to the General Secretary of the BIR for application to either of the visits below.

**Stockholm:** to the clinic of the late Dr Curt Westman, now owned by AB Medicinsk Roentgen.

**Paris:** to radiotherapy centres in Paris, arranged through the collaboration of Professor M Tubiana

**Clinical Usefulness of Nuclear Medicine Image Processing**
February 9, 1988
Joint IPSM/BIR meeting organised by the IPSM.
Further details: General Secretary, IPSM, 2 Low Ousegate, York YO1 1QU (Tel. 0904-610 821).

**Functional Insights From Magnetic Resonance**
February 17, 1988
London, venue to be confirmed
Organised by the Diagnostic Methods Committee.
Chairmen: Prof. B. S Worthington and Dr G Bydder
Speakers. Dr M. A. Smith, Mr D Longmore, Prof P. Mansfield, Dr I Young, Dr Hadley, Prof. I. Isherwood, Dr S. Williams, Dr Edwards, Dr B Ross, Prof O. Reynolds, Dr J Cox and Dr V. R. McReady

This meeting will incorporate the 1988 **Silvanus Thompson Memorial Lecture,** which will be open to non-registrants

**Radiobiology All-Day Non-topic Proffered Papers Meeting**
February 19, 1988
Organised by the Radiobiology Subcommittee.

**New Demands on Diagnostic Equipment to Reduce Radiation Dose**
March 9, 1988
London, venue to be confirmed
All-day meeting organised by the Industry and Radiation Protection Committees.
Chairman· Dr J. G Russell

**Total-Body Irradiation**
April 13, 1988
Joint BIR/IPSM meeting organised by the BIR.

**Conversazione**
June 23, 1988
Institute of Directors, London SW1

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**32 Welbeck Street revisited**
32 Welbeck Street, the Institute's old home, now occupied by the Variety Club of Great Britain, has been renovated and the lecture theatre restored to something like its former glory as a Russian orthodox church (see the June 1986 *Bulletin,* B35) Members who would like to visit Welbeck Street are welcome to call

# Library news

**The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)**

*The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).*

*The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the* Bulletin. *Most books (excepting the historical collection) are available on loan.*

*There is an agreement which allows BIR members limited use of the RSM Library for reference purposes. Members should apply to the BIR Librarian for a visitor's card.*

**Recent additions to the Library**

Collier, J. G. & Davies, L M. Chernobyl. Central Electricity Generating Board. 1986
Faerber, E. N Cranial computed tomography in infants and children. 1986
Goddard, P. R: Diagnostic imaging of the chest 1987
HMSO: Committee on medical aspects of radiation in the environment First report 1986
ICRU Report 40. The quality factor in radiation protection. 1986
NCRP Report 83: The experimental basis for absorbed dose calculations in medical uses of radionuclides. 1985
Otto, R. C. & Higgins, C. B. (Eds): New developments in imaging 1986

New periodicals.
Journal of thoracic imaging
Journal of ultrasound in medicine
Seminars in interventional radiology

**Scientific documents**

British Standards Institution. *Specification for Sterile Intravascular Cannula Units for Single Use. Gr6.* BS4843: 1987

British Standards Institution *Medical Electrical Equipment. Part 2: Particular requirements for the safety of therapeutic X-ray generators.* IEC 601-2-8

These documents are now filed in the Library.

# Meetings and courses

*As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion Please contact the Managing Editor.*

**The Bart's MCQ Course (FRCR II)**
September 1, 1987
St Bartholomew's Hospital, London
Further details Mrs C. Burrage, MCQ Course Secretary, Room 26 Dunn Laboratories, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE (Tel. 01-601 7531)

**Paediatric Radiology Course**
September 2–4, 1987
Further details Dr G M. Steiner, Sheffield Children's Hospital, Western Bank, Sheffield S10 2TH (Tel. 0742-761111).

**Current Dilemmas in Gynaecological Oncology**
September 3–5, 1987
University of Birmingham
Further details· Conference Organiser (ONC), Bell Howe Conferences, Gothic House, Barker Gate, Nottingham NG1 1JU (Tel 0602-410 679).

**St Bart's Megavoltage Radiotherapy 50th Anniversary Conference**
September 3–5, 1987
St Bartholomew's Hospital, London
Further details The Secretariat, Concorde Services, 10 Wendell Road, London W12 9RT.

**1st Biennial Brachytherapy and Remote Afterloading Symposium and Workshop**
September 14–16, 1987
St Louis, Missouri, USA
Further details. Carlos A Perez, M D, Symposium Chairman, Director, Radiation Oncology Center, Mallinckrodt Institute of Radiology, 4511 Forest Park Boulevard, Suite 411, St Louis, Missouri 63108, USA (Tel. 314-362 3497)

**Intra-operative Ultrasonography**
September 18–19, 1987
Paris, France
Further details. Convergences, 16 rue Jean Jacques Rousseau, 75001 Paris, France

**RCR Annual Meeting and Annual General Meeting**
September 24–26, 1987
John Radcliffe Hospital, Oxford
Incorporating the Joint Autumn Provincial Meeting of the RCR, the BIR and the Radiology Section of the RSM
Further details The Conference Officer, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG (Tel 01-636 4432/3)

**Radiology and Management of Trauma Course**
12–15 October, 1987
Leicester Royal Infirmary
Further details Dr D. Finlay, Consultant Radiologist, Leicester Royal Infirmary, Leicester LE1 5WW.

**6th Symposium on Neutron Dosimetry**
October 12–16, 1987
Neuherberg, Federal Republic of Germany
Further details. GSF Munchen, Institut fur Strahlenschutz, Dr H Schraube, Ingolstadter Landstr. 1, D-8042 Neuherberg, Federal Republic of Germany (Tel. 089-31 87 (0) 3349)

**RCR Interventional Radiology Course**
October 13–15, 1987
Hotel St George, Sheffield
Further details. Dr D C Cumberland, Consultant Radiologist, Northern General Hospital, Sheffield S5 7AU (Tel 0742-434 343 ext. 4828)

**4th International Symposium on Diagnostic Imaging**
October 19–23, 1987
Barcelona, Spain
Further details Núria de Arana, c/o Centro Radiologico Computarizado de Barcelona, Tavern, 82, 08006 Barcelona, Spain.

**Principles and Practice of Radiotherapy**
October 26–29, 1987
Ljubljana, Yugoslavia
Further details European School of Oncology, Via Venezian 1, 20133 Milan, Italy (Tel 02 235 923-266 4662).

**9th London Ultrasound Course**
November 9–13, 1987
Skyway Hotel, Hayes, Middlesex
Further details Dr H B Meire, X-ray Department, King's College Hospital, Denmark Hill, London SE5 9RS.

**International Symposium on New Developments in Head and Neck Cancer**
December 2–4, 1987
Free University, Amsterdam, the Netherlands
Further details: Prof Dr G. B. Snow, Department of Otolaryngology, Free University Hospital, de Boelelaan 1117, 1081 HV Amsterdam, the Netherlands.

**Breast Imaging 1988**
February 1–5, 1988
United States Virgin Islands
Further details Harvard Continuing Education, Boston, MA 02114, USA (Tel. 617-732 1525)

**6th International Meeting on Chemical Modifiers of Cancer Treatment**
March 21–25, 1988
Paris, France
Further details Dr E. P Malaise, Laboratoire de Radiobiologie Cellulaire (Unité Inserm 247), Institut Gustave-Roussy, 94805 Villejuif Cedex, France.

**The London Course in Whole Body Computed Tomography**
March 27–31, 1988
Gleneagles Hotel, Scotland
Further details. Mrs Janice O'Donnell, Course Secretary, Dept of Radiology, Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT.

**ISPRAD V: 5th Meeting of the International Symposium on the Planning of Radiological Departments**
April 20–23, 1988
Florence, Italy
Further details. Dr Antonio Chiesa, Cias Editoriale, Via Pace, 8-25122 Brescia, Italy

**14th L.H. Gray Conference. Low Dose Radiation—Biological Bases of Risk Assessment**
September 11–15, 1988
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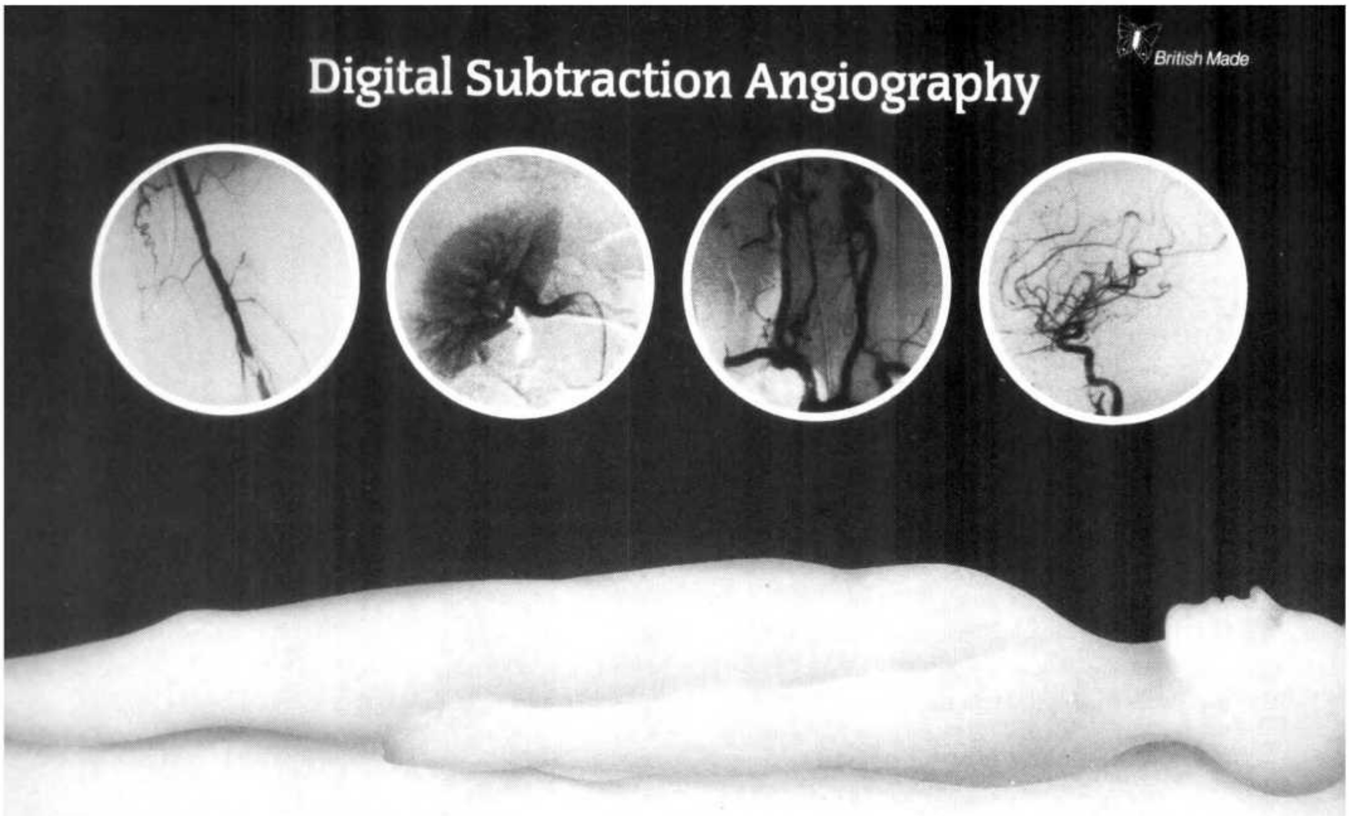

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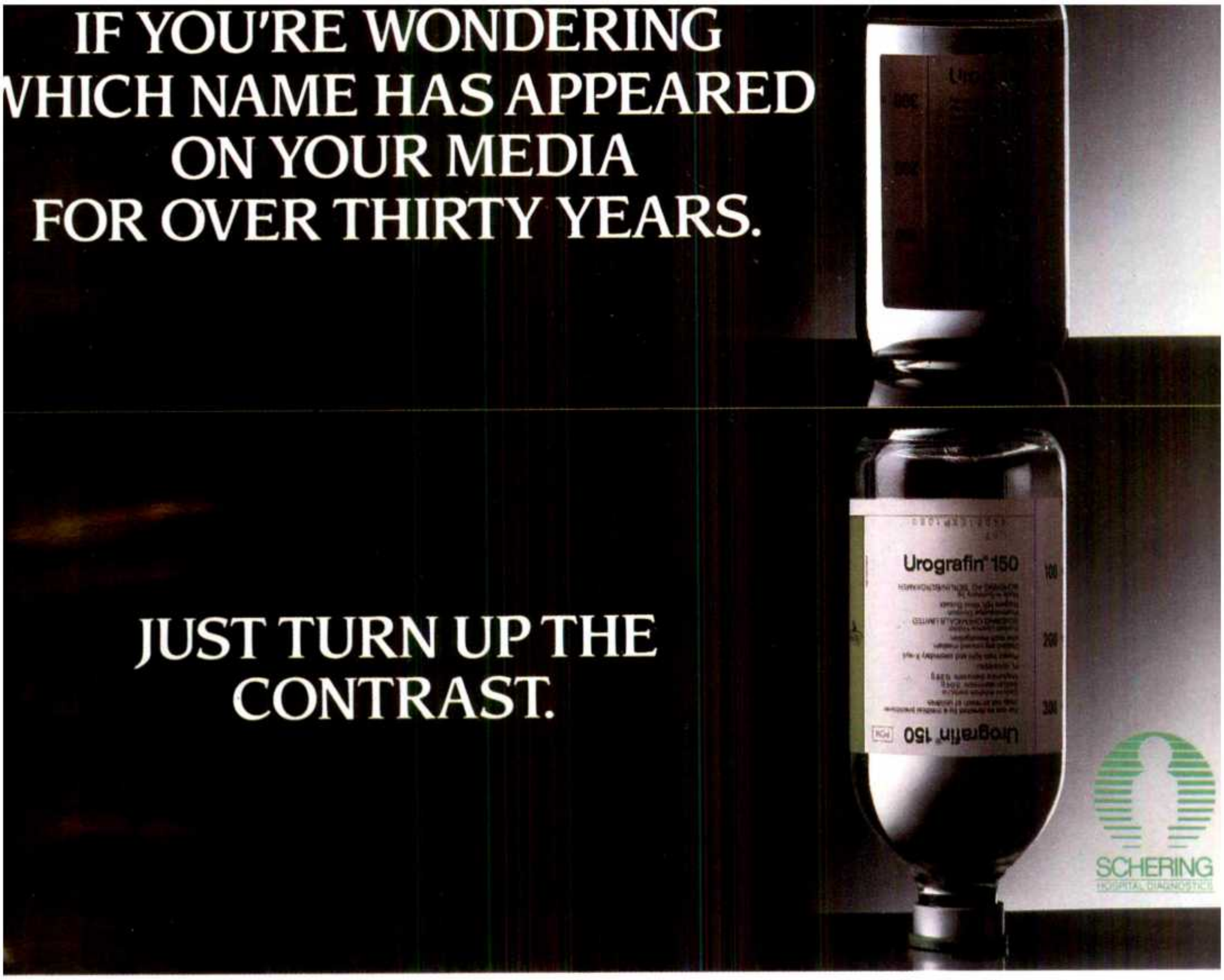

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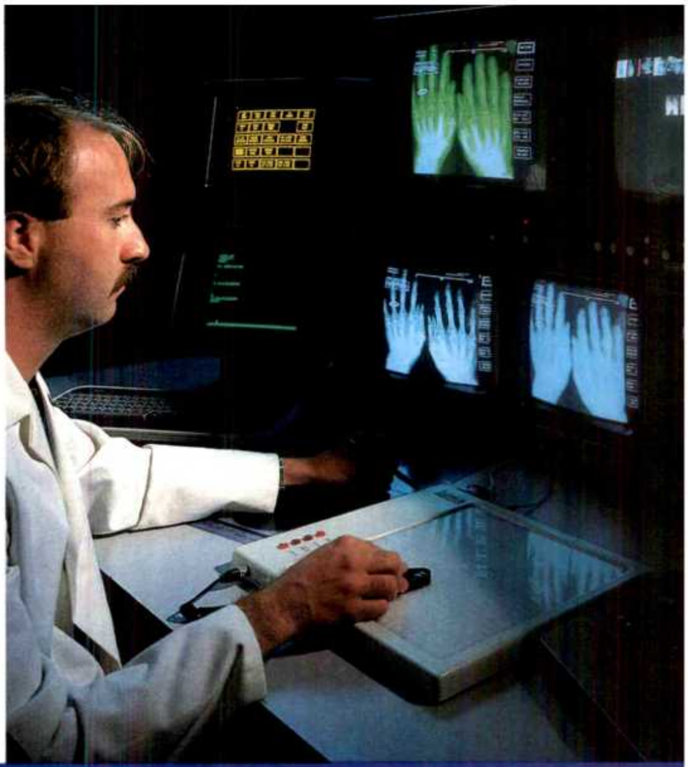

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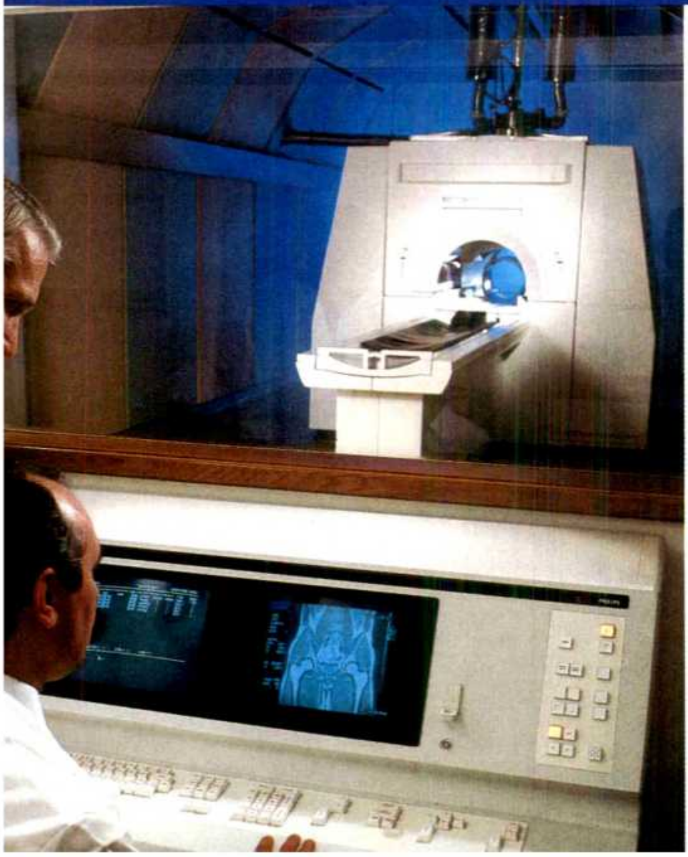

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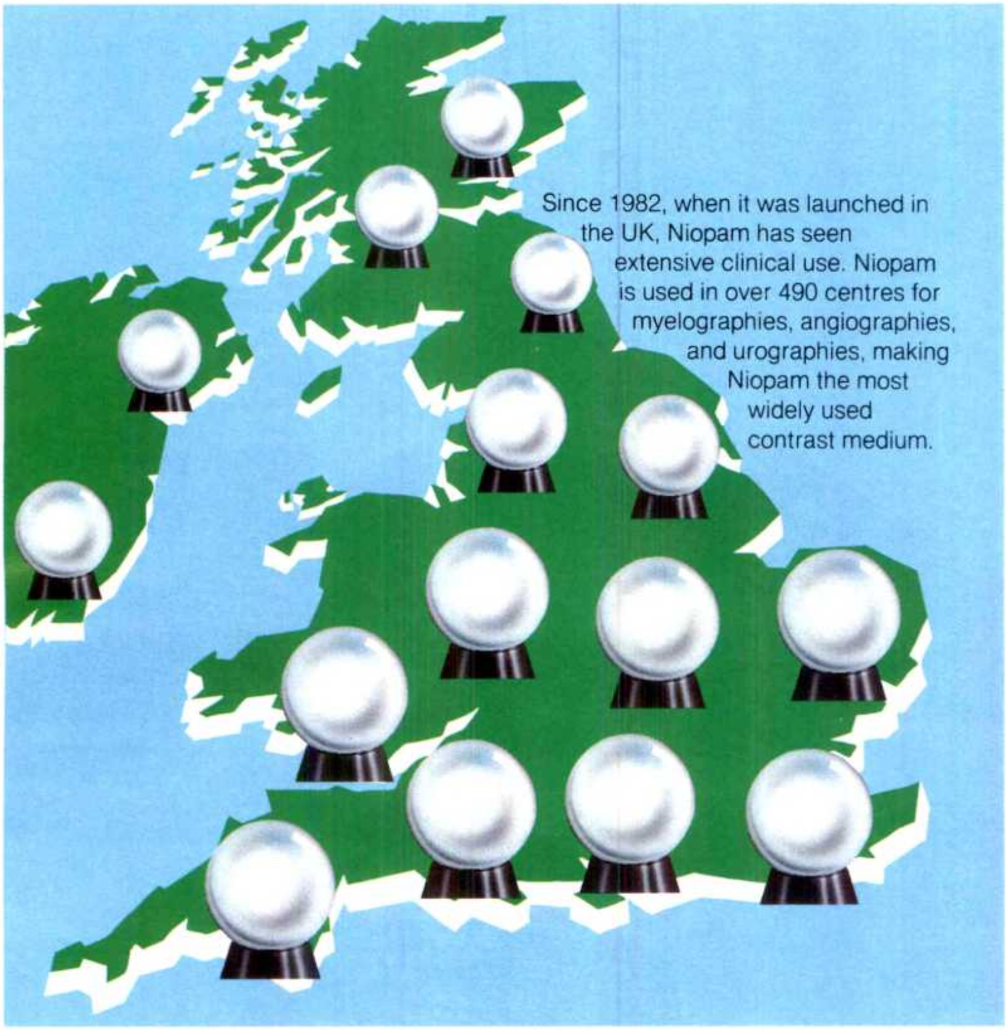
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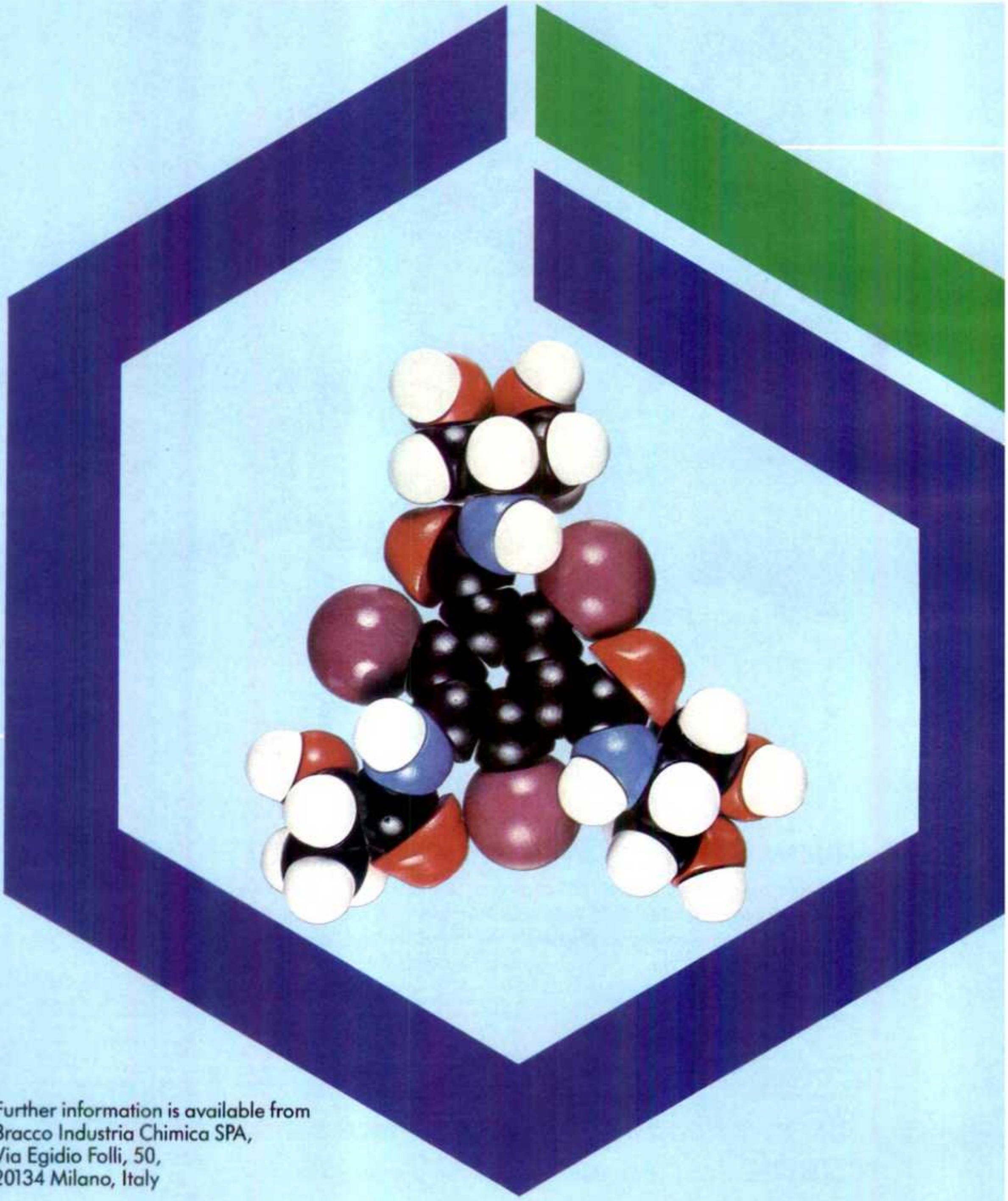

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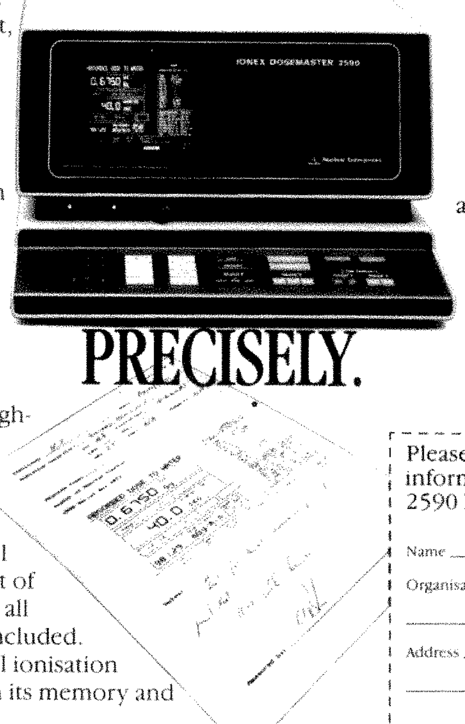

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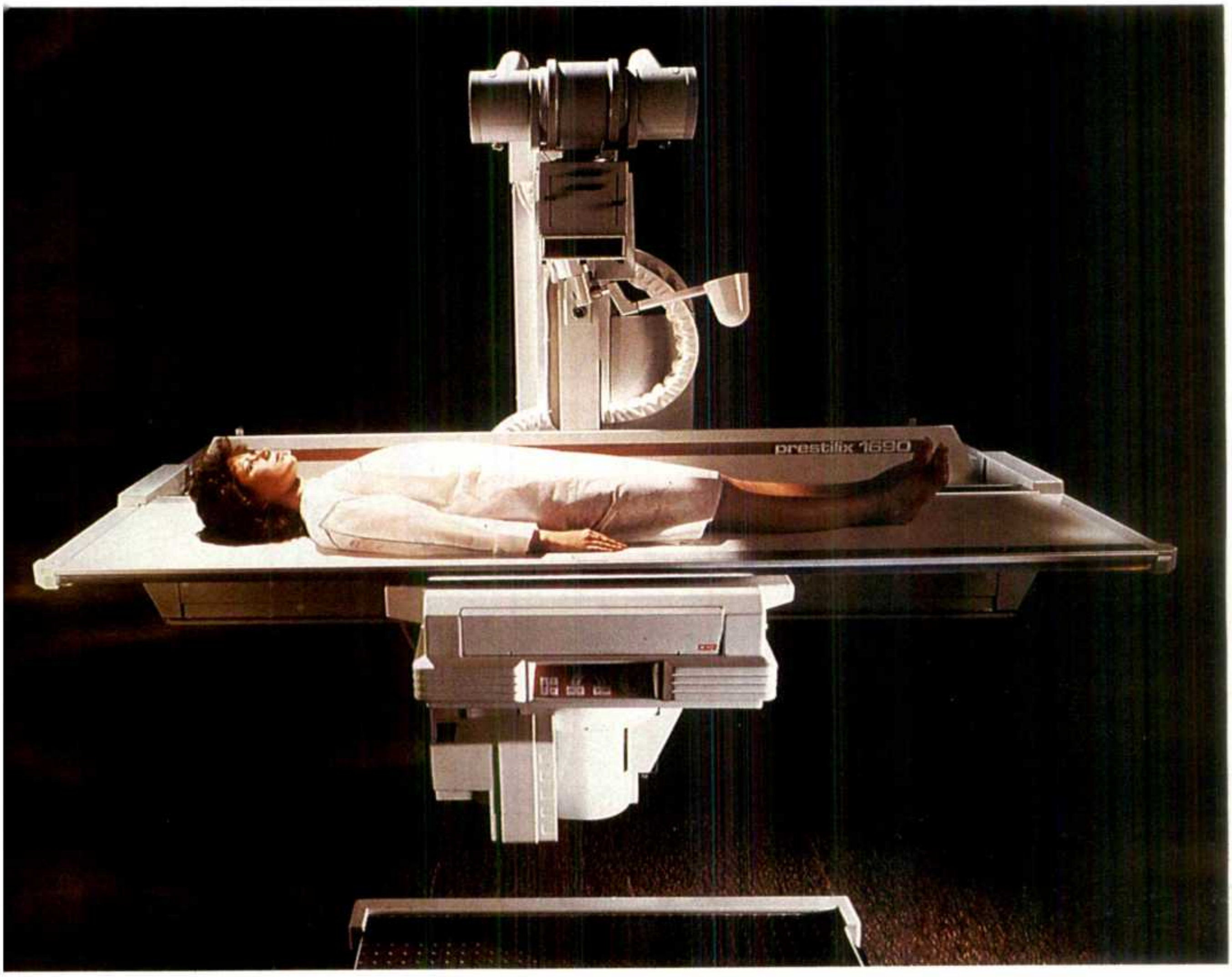

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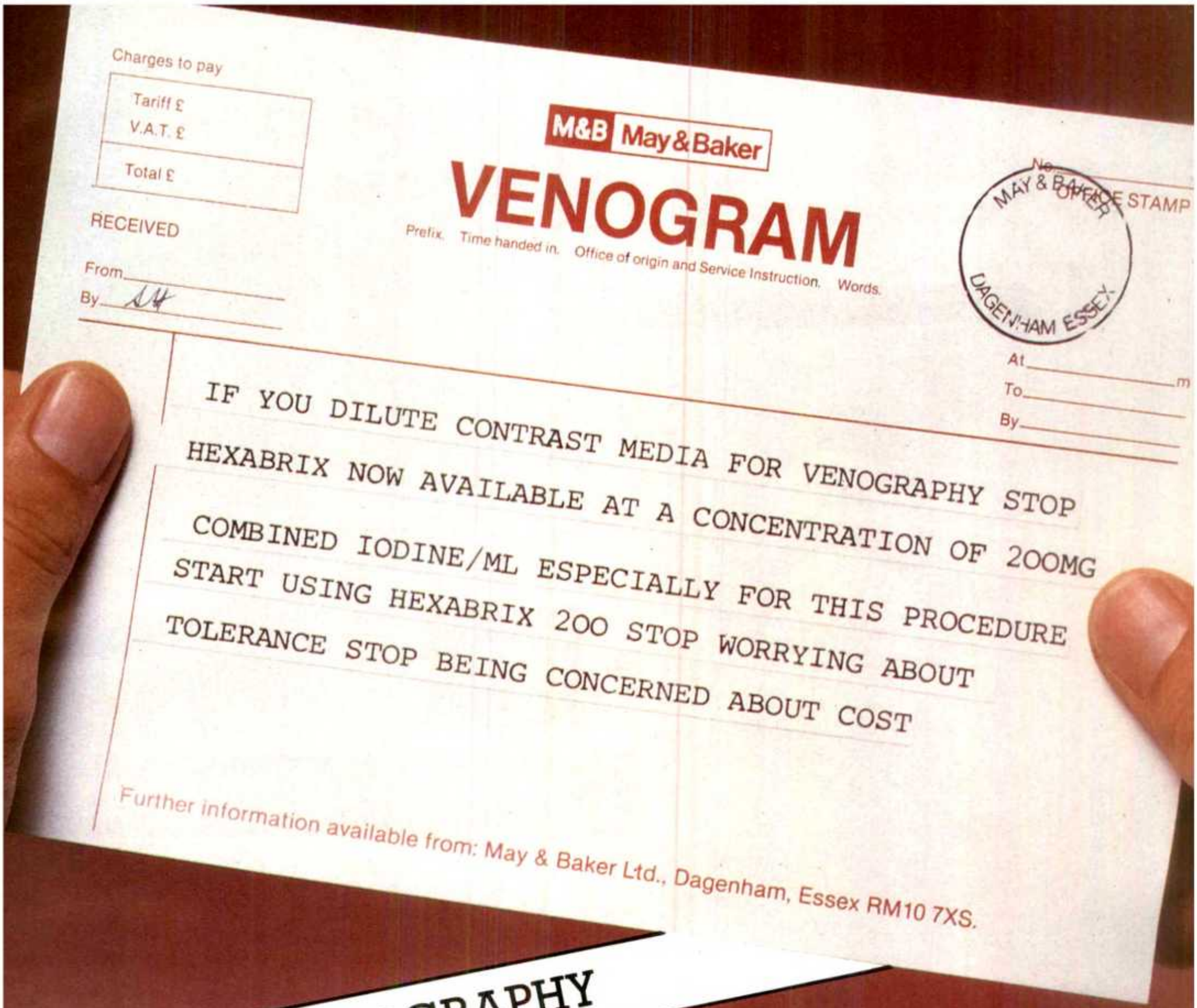

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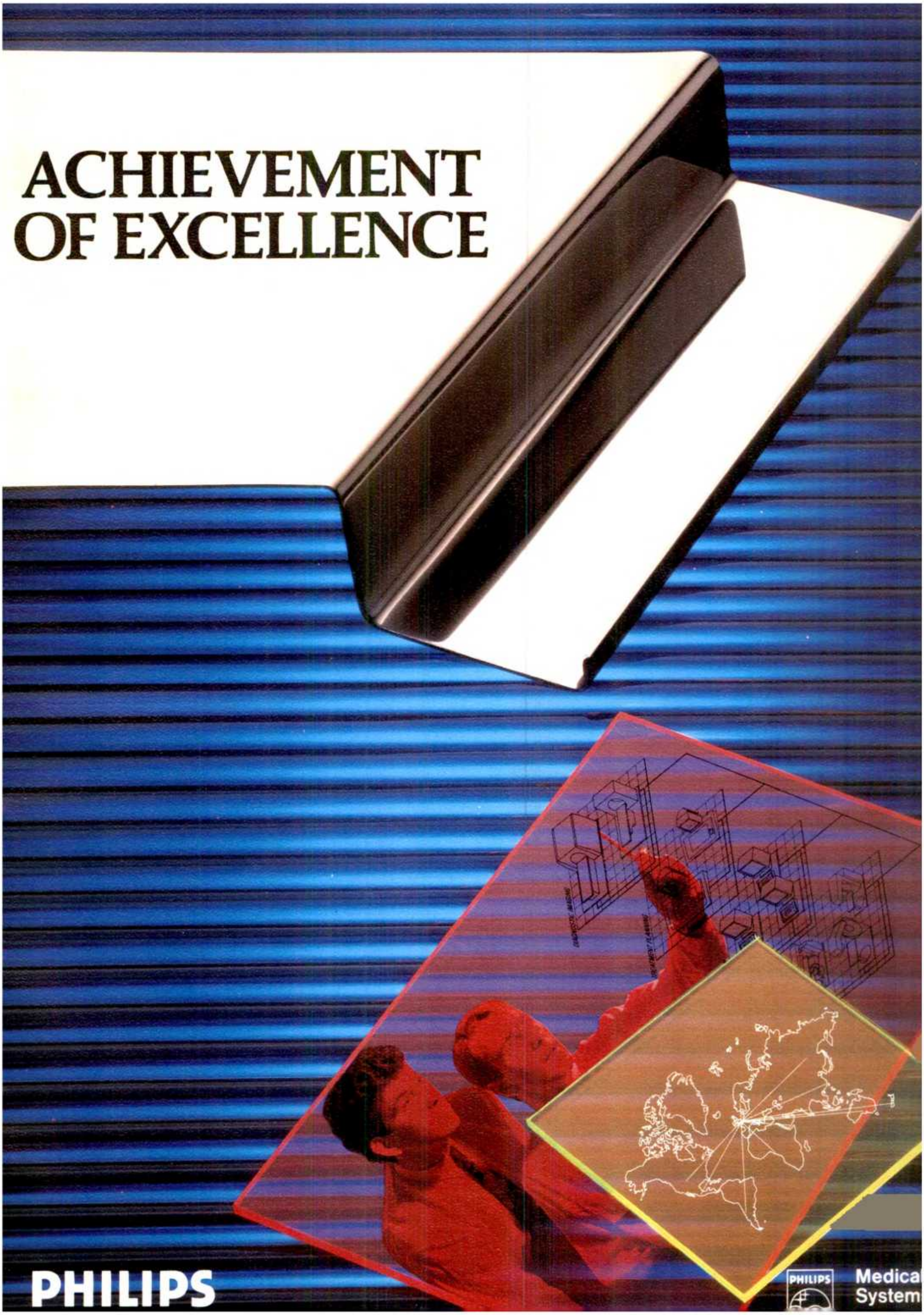
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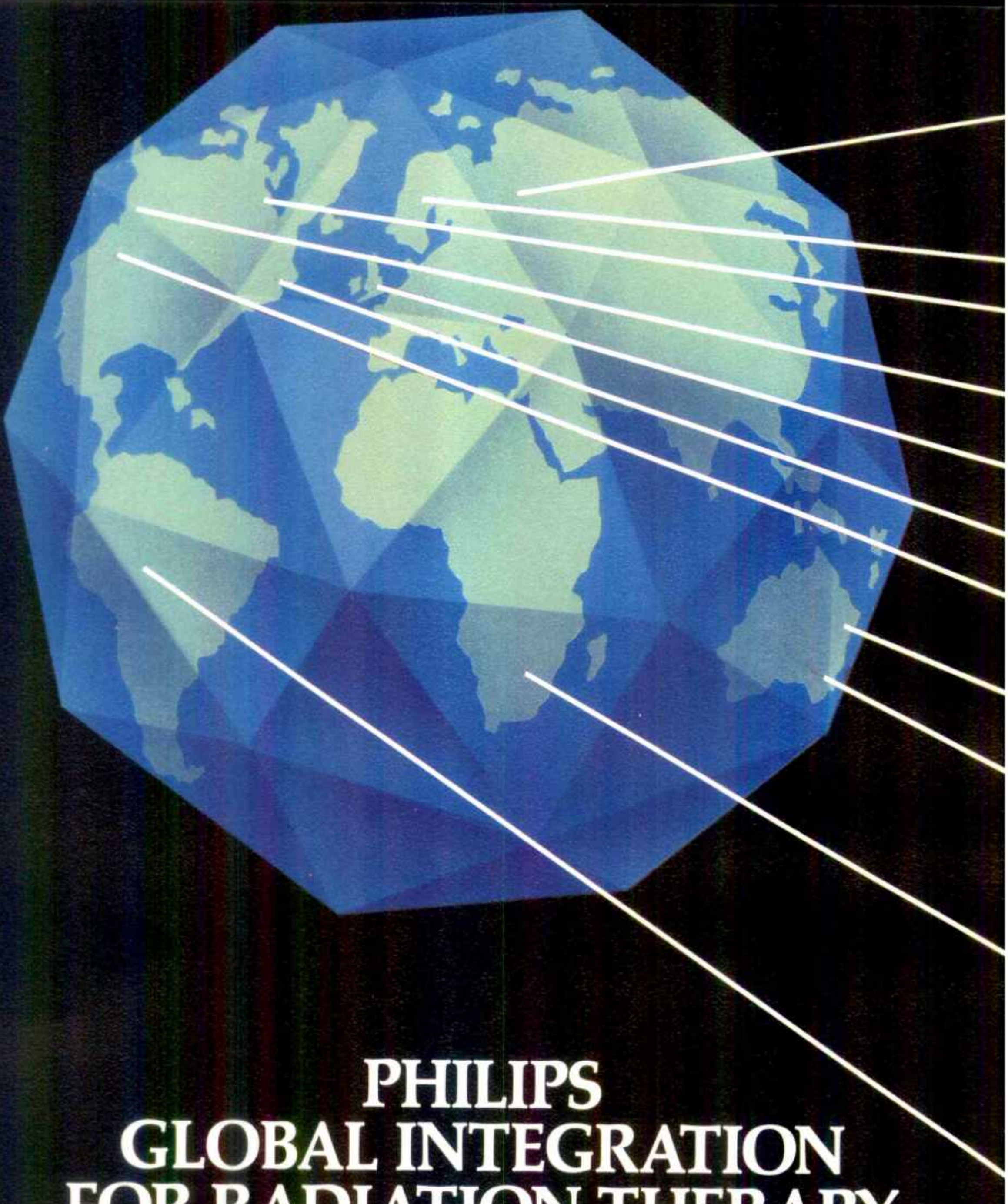

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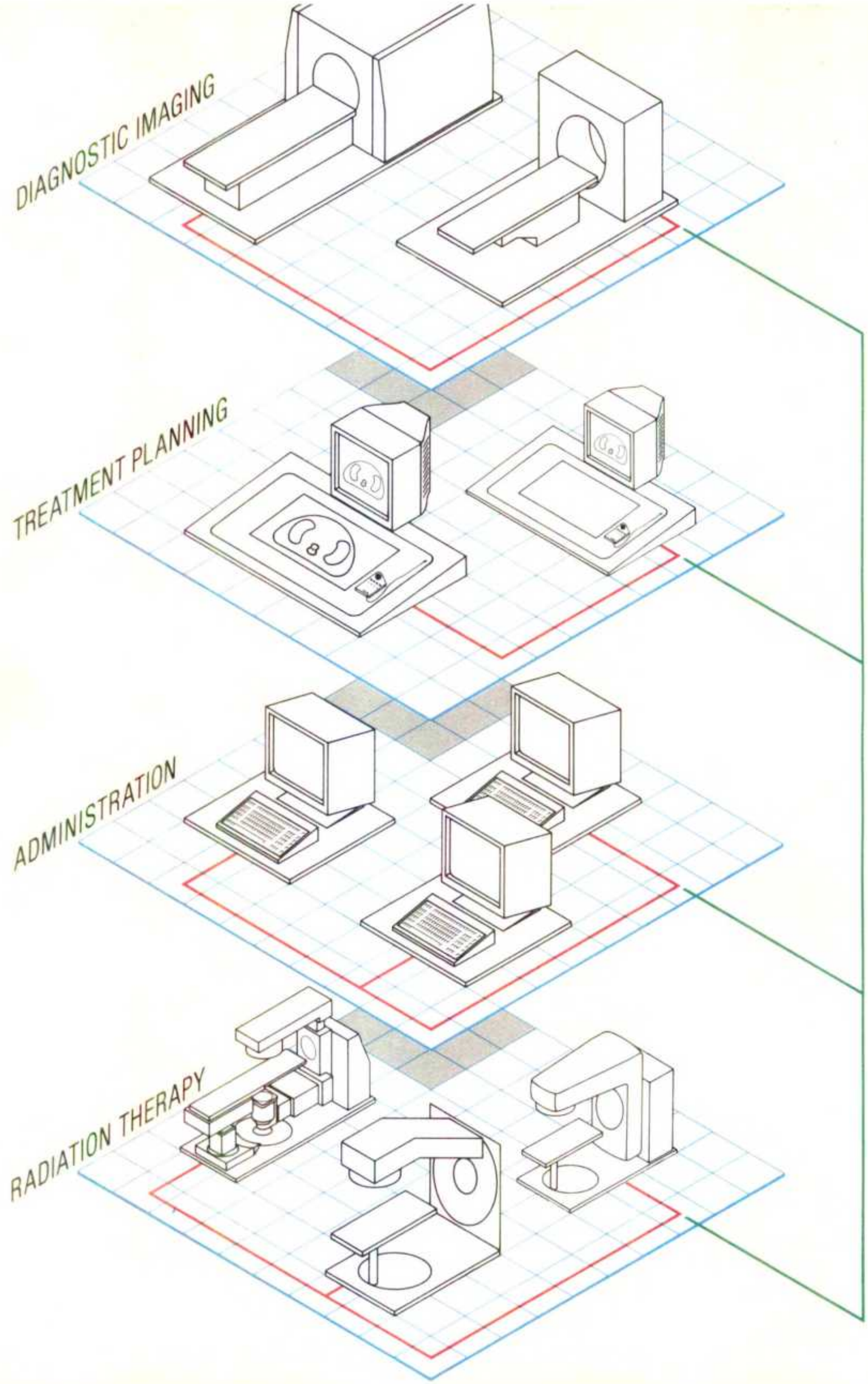

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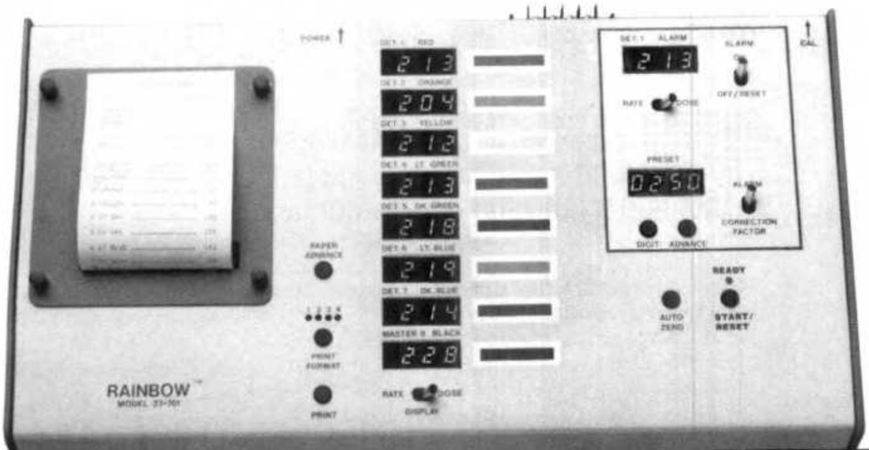

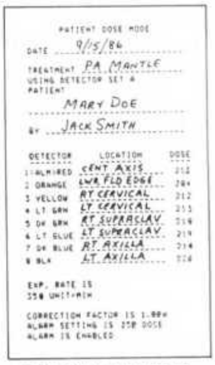

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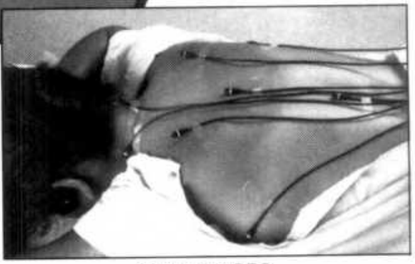

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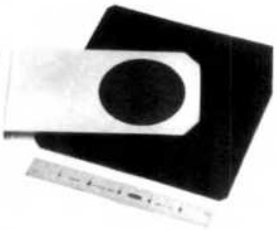

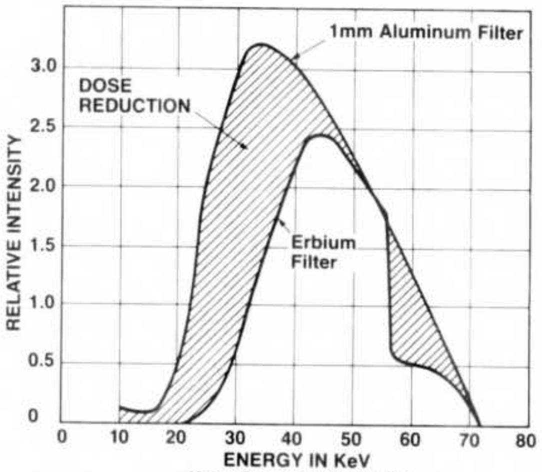

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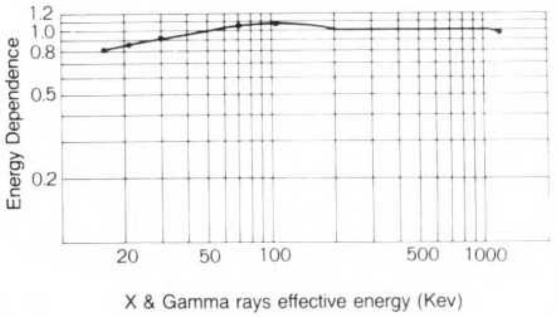

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1987, *The British Journal of Radiology*, 60, 849–860

VOLUME 60 NUMBER 717 SEPTEMBER 1987

The British Journal of Radiology

# Radiological assessment of Paget's disease of bone after treatment with the bisphosphonates EHDP and APD

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*(Received June 1986 and in revised form January 1987)*

## ABSTRACT

The effects of therapy on the osteolytic bone lesions of Paget's disease have been assessed from serial bone radiographs. Changes in the rate of progression of lytic "wedge" lesions were measured and alterations in the texture of lytic "blade" lesions were graded on an empirical scale. Useful matching was possible using standard radiographs, although special care was needed to avoid artefacts from suboptimal positioning, magnification and variation in exposure Serial radiographs were obtained of 57 lytic blade lesions in 54 patients receiving treatment with the bisphosphonate 1-hydroxyethylidene-1, 1-bisphosphonate (EHDP) and of 20 lesions in 20 patients treated with oral or intravenous 3-amino-1-hydroxypropylidene-1, 1-bisphosphonate (APD). Treatment with EHDP was associated with a significant deterioration in bone texture in 50% of lytic blade lesions, and with healing in only 20% Deterioration was accompanied by an increase in local bone pain in 17% of these patients. In contrast, significant healing was observed in 17 of 20 lytic lesions (eight wedge, nine blade) within 6 months of beginning a course of intravenous or oral APD. In four of eight patients the progression of a lytic tibial wedge was arrested and in the remaining four the direction of wedge movement was reversed In two patients the wedge had almost completely "filled in", making measurement difficult. Bone healing was usually accompanied by pain relief, reduction in skin temperature and rapid suppression of the urine hydroxyproline (uHP) into the normal range. However, in four patients who received intravenous APD, repair of lytic bone lesions was observed despite persisting elevation of uHP. These improvements with APD were sustained at 12 months, although in one patient whose biochemical indices were restored to normal the resorption front showed further progression, despite initial temporary reversal. The trends apparent in these short-term studies were also seen in four patients in whom wedge velocities were measured over periods of 6–10 years. These results confirm that after treatment of Paget's disease, bone healing or deterioration can be accurately assessed from serial standard radiographs. Reproducible matching is best achieved by ensuring that all radiographs are taken by the same radiographer Minor alterations in radiological bone texture provide an important index of drug effect which is not always apparent from measurement of biochemical and other indices.

The availability of potent therapeutic agents such as calcitonin and the bisphosphonates, which are capable of promoting bone healing in Paget's disease, has focused attention on methods of assessing treatment in this condition Changes in biochemical indices of disease activity, although easily measured, may not always reflect bone events. For example, with calcitonin therapy, radiological healing of bone may occur despite only partial biochemical suppression (Nagant de Deuxchaisnes et al, 1977), and with 1-hydroxyethylidene-1, 1-bisphosphonate (EHDP) a paradoxical deterioration in bone morphology may follow restoration of biochemistry to normal (Nagant de Deuxchaisnes et al, 1979). Similar discrepancies occur with qualitative bone scintigraphy, which can show apparent improvement with EHDP despite evidence of radiological deterioration (Nagant de Deuxchaisnes et al, 1980).

Although less common than osteosclerosis, the lytic bone lesion is more easily measured. Assessment of bone healing in serial radiographs is, however, dependent, on the strict comparability of radiographs. Such precision is possible in a specialist unit (Nagant de Deuxchaisnes et al, 1977) but is not easily achieved under routine conditions. The present study of osteolytic Pagetic bone lesions was undertaken to assess the feasibility of such assessment in a service radiology department. Retrospective data obtained in patients treated with EHDP were analysed and compared with more recent and closely monitored radiographs from patients receiving 3-amino-1-hydroxypropylidene-1, 1-bisphosphonate (APD).

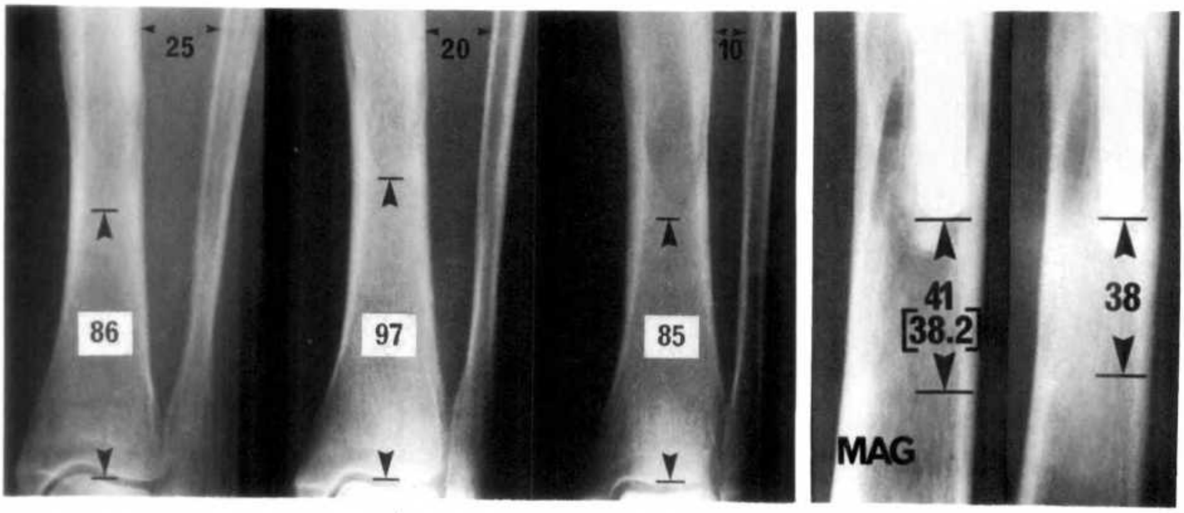
## METHODS

### *Biochemical evaluation*

Serum alkaline phosphatase (sAP) and urine hydroxyproline (uHP) were measured by the methods of Bowers and McComb (1966) and Zender (1972) respectively. Excretion of uHP was expressed as a ratio with urine creatinine (uHP/Cr); normal = 5–30 μmol/mmol.

### *Radiographic evaluation*

Matched radiographs were usually taken by the same radiographer at approximately 6-month intervals.



A

B

Fig. 1.

(A) Effect of rotation of bone on apparent wedge progression. The central radiograph represents the optimal position for matching. Minor rotation in the left and right hand radiographs taken at the same time has resulted in an underestimate of wedge distance by 10 mm and 20 mm respectively. (B) Apparent alteration in wedge distance resulting from magnification in the radiograph on the left. Correction of the distance by the bone width ratio gives an estimate of the true value (38.2 mm).

Because accurate positioning was more easily achieved with skull and tibial lesions, the study was confined mainly to radiographs of these two bones. Exposures were standardised on the same X-ray unit with accurate automatic exposure control. Details of kV, filtration and screen-film combination were recorded for future duplication. Exposure consistency was checked by an aluminium step-wedge included on each radiograph and accurate matching was ensured by a preliminary check radiograph. Cortical lytic areas were arbitrarily classified as "blade" and "wedge" lesions. Blade lesions included linear cortical clefts and patchy osteolytic

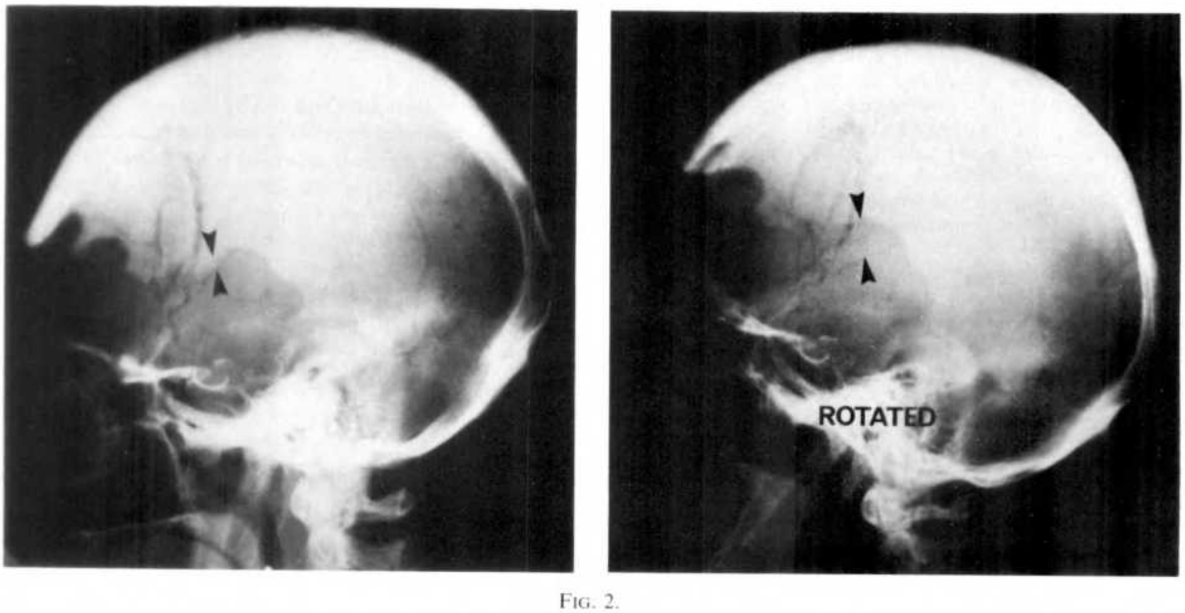


Fig. 2.

Effect of rotation of the skull on the apparent area of lysis. Rotation of the skull in the lower radiograph has resulted in apparent increase in the lytic area (arrow heads).

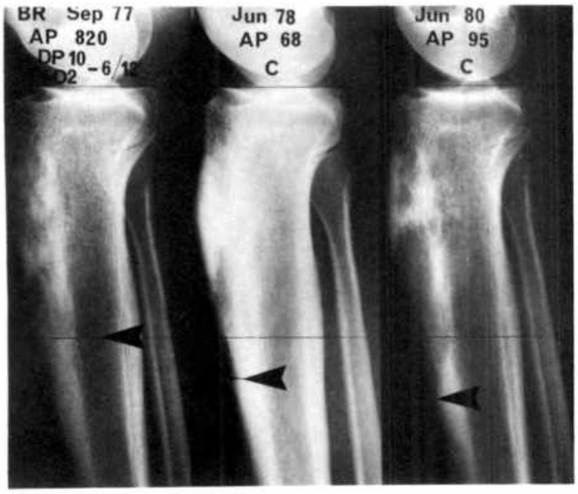


FIG. 3.

Underexposure in the radiograph of June 1978 suggests apparent improvement in bone texture, despite wedge progression. DP 10 = EHDP 10 mg/kg/day, $D_2$ = vitamin $D_2$, C = control, AP = serum alkaline phosphatase.

areas in which there was no clearly defined lytic front. Deterioration or improvement in bone texture was assessed on an arbitrary scale of 1 to 4, 1 representing a slight but discernible change from the index radiograph and 4, complete or almost complete restoration to normal. Changes in the position of wedge-shaped osteolytic resorption fronts were measured from a fixed point in millimetres (wedge distance) or in millimetres per month (wedge velocity).

Radiographs were assessed blind by two observers independently and agreement was recorded in 88% of the radiographs at the first assessment. In the remaining 12% a mean figure for wedge distance and velocity was used. In the retrospective analysis of radiographs from EHDP-treated patients, 22% of radiographs were excluded because of minor variations in technique which made measurement of wedge distance unreliable (Fig. 1A,B), (all but four patients), areas of lytic involvement (Fig. 2) or alteration in bone texture (Fig. 3).

*Patients and therapy*

Radiographs of 57 lytic blade lesions in 54 patients treated with EHDP were obtained over periods of 6–28 months. In a prospective study, 20 lesions in 20 patients were compared before and at 6 and 12 months after a course of APD. In four patients, lytic tibial resorption fronts (wedges) were measured during successive courses of EHDP, calcitonin, EHDP/calcitonin and APD over periods of 6–19 years. EHDP was given in a standard oral dose of 10 mg/kg/day for 6 months. APD was given either as an oral dose of 10 mg/kg/day for 6 months (15 patients) or as a daily 2 h intravenous infusion (0.25–0.375 mg/kg) for 5 or 10 days (five patients).

## RESULTS

*EHDP therapy*

Both healing and deterioration of lytic lesions were seen with this drug. Healing occurred infrequently in peripheral bones and was seen more often in pure lytic lesions in the skull (Fig. 4). Radiological deterioration involved both cortical and trabecular bone and was associated with an increase in bone pain in five out of 29 patients and, in one instance, with a fracture (Fig. 5). Deterioration occurred mainly in pre-existing Pagetic lesions, though linear lytic areas (blade lesions) occasionally appeared during treatment in apparently normal cortical bone. Deterioration in the radiographic appearance was usually arrested when treatment was stopped and was often followed by healing with bone of apparently normal texture. This was, however, often delayed for longer than 6 months.

The results of the analysis of radiographs of 57 lytic blade lesions before and after a 6-month course of

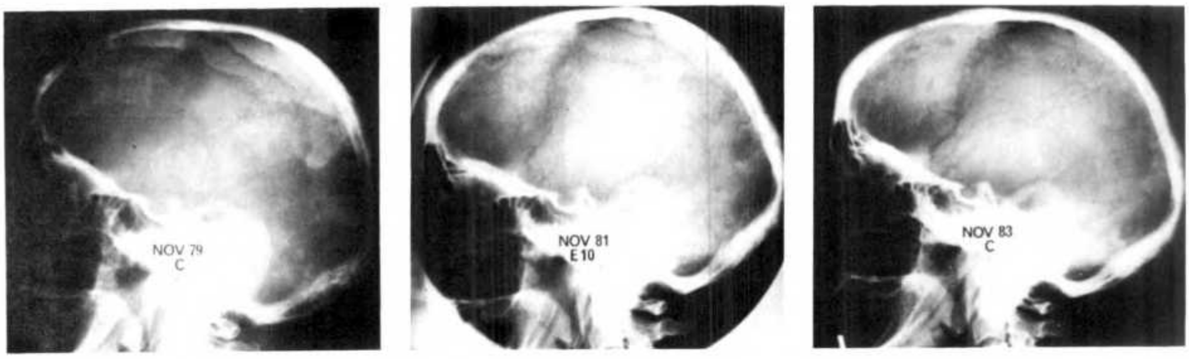


FIG. 4.

Almost complete healing of lytic skull lesions following a 6-month course of EHDP (E10) 10 mg/kg given between January and June 1981.

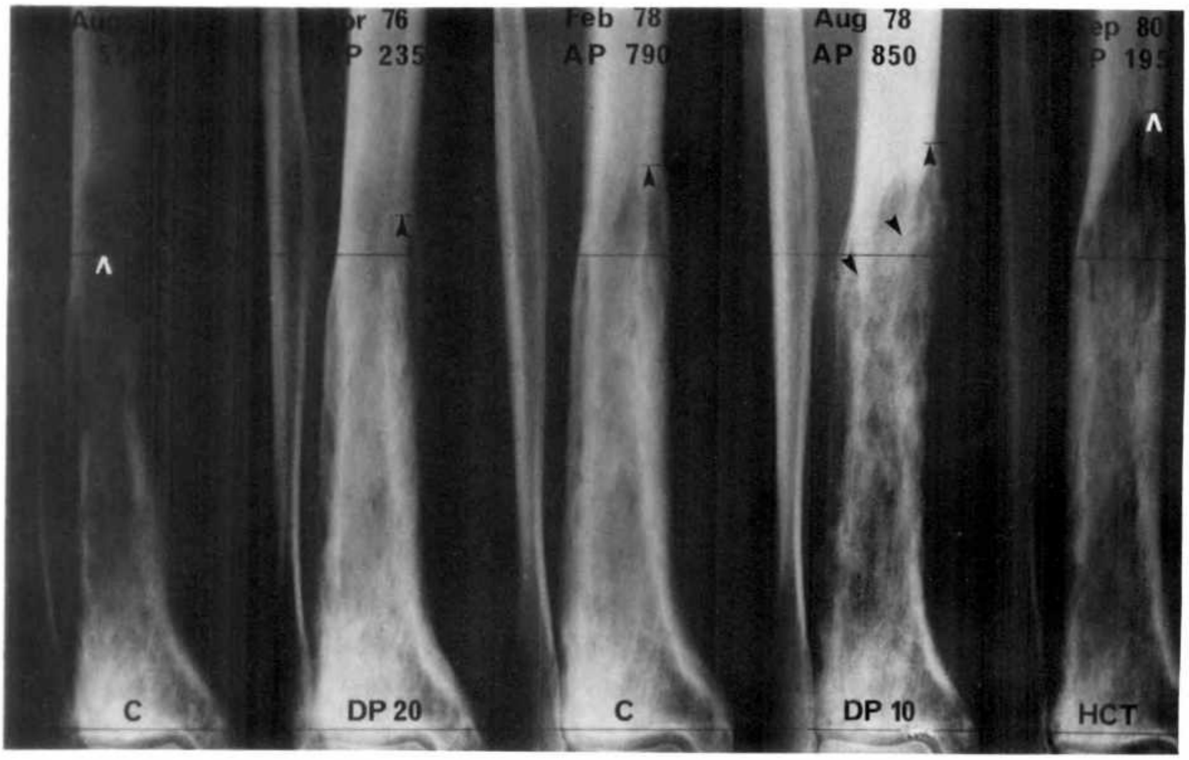


FIG. 5.

Upward progression of the lytic wedge during (April 1976) and following (February 1978) a 6-month course of EHDP (DP 20) 20 mg/kg/day. Further progression, linear demineralisation and fracture (diagonal arrowheads) occur during (August 1978) and after further treatment with EHDP in a dose of 10 mg/kg/day. HCT = human calcitonin.

EHDP are shown in Table I. Therapy was associated with radiological deterioration in 50% of the lytic areas and signs of healing were observed in only 11 (19%). In four patients with pure lytic areas in the skull the lesions disappeared completely.

These radiographic changes were independent of the biochemical response. There was a reduction in biochemical indices of disease activity in all patients and 70% were judged to be in biochemical remission (uHP/Cr < 30 μmol/mmol) at the end of the 6-month course of therapy. Radiological deterioration occurred in patients who were in either partial or complete remission.

TABLE I

THE EFFECT OF EHDP THERAPY ON OSTEOLYTIC BONE LESIONS

| | No. of lesions | | | |
|---|---|---|---|---|
| | Total | Healing | Deterioration | No change |
| Skull | 26 | 5 | 13 | 8 |
| Tibia | 18 | 5 | 10 | 3 |
| Other | 13 | 1 | 6 | 6 |
| Totals | 57 | 11 | 29 | 17 |

### *APD therapy*

In contrast to the predominantly deleterious effect of EHDP on lytic lesions, APD caused partial or complete healing of lytic blades or wedges in 17 out of 20 patients at the end of the 6-month therapy period (Table II). The pattern of wedge repair varied in different lesions. In some, arrest of wedge progression was accompanied by "filling in" of proximal lytic cortical areas (Fig. 6), while in others more obvious repair occurred at the apex of the wedge, with resultant reversal of the direction of movement. In the remainder, there was generalised filling in of the whole wedge, which prevented accurate repeat measurement. There was good agreement between radiological healing and biochemical response, although in four patients, healing occurred despite only partial biochemical remission (Fig. 7). In one patient there was definite deterioration in a lytic lesion in the right tibia, which was accompanied by only a small reduction in uHP/Cr to a level which was still elevated three times above the upper limit of normal.

TABLE II

LYTIC WEDGE ANALYSIS BEFORE AND AFTER 6 MONTHS OF THERAPY WITH APD

| Case | Age (years) | Sex | Bone | Wedge velocity (mm/month)* | | | Cortical texture† | | uHP/Cr ratio‡ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Baseline | 6-month | 12-month | 6-month | 12-month | Baseline | 6-month | 12-month |
| A | 54 | M | Tibia | +0.3 | H | −0.5 | + | ++ | 239 | 174 | 175 |
| B§ | 62 | M | Tibia | −0.3 | −0.4 | −0.4 | + | + | 124 | 4 | 25 |
| C | 73 | M | Tibia | +0.5 | −0.3 | H | ++ | +++ | 156 | 92 | 91 |
| D | 61 | M | Tibia | +0.6 | −0.4 | +0.2 | ++ | ++ | 78 | 18 | 16 |
| E | 71 | M | Tibia | +1.3 | 0 | −1.1 | + | ++ | 81 | 10 | 12 |
| F | 70 | F | Tibia | +1.5 | −0.7 | H | ++ | ++++ | 64 | 16 | 21 |
| G | 55 | F | Femur | +0.6 | −0.6 | 0 | + | ++ | 47 | 21 | 11 |
| H | 59 | M | Femur | +0.1 | H | H | +++ | +++ | 146 | 54 | 123 |

* + = wedge progression, − = wedge regression, H = healed (resorption front no longer measurable).

† + = slight improvement, ++ = moderate improvement, +++–++++ = normal to almost normal bone texture.

‡ uHP/Cr = urine hydroxyproline excretion ($\mu$mol per mmol creatine); normal = 5–30 $\mu$mol/mmol.

§ In this patient, regression of the wedge was already in progress following a previous course of calcitonin.

In eight patients, wedge velocity was measured before treatment (Table II). After 6 months, the wedge had either arrested or disappeared in four patients and reversed its direction in the remaining four. After a further 6 months without treatment these improvements were sustained and three wedges had disappeared. In one patient (Figs 8, 9) further slight downward progression of a tibial lytic wedge occurred despite its previous reversal at 6 months. This patient was in complete biochemical remission (uHP/Cr <30 $\mu$mol/mmol) but local warmth over the tibial lesion indicated continuing disease activity.

LONG-TERM STUDIES

The availability of suitably matched radiographs made possible a retrospective assessment of wedge

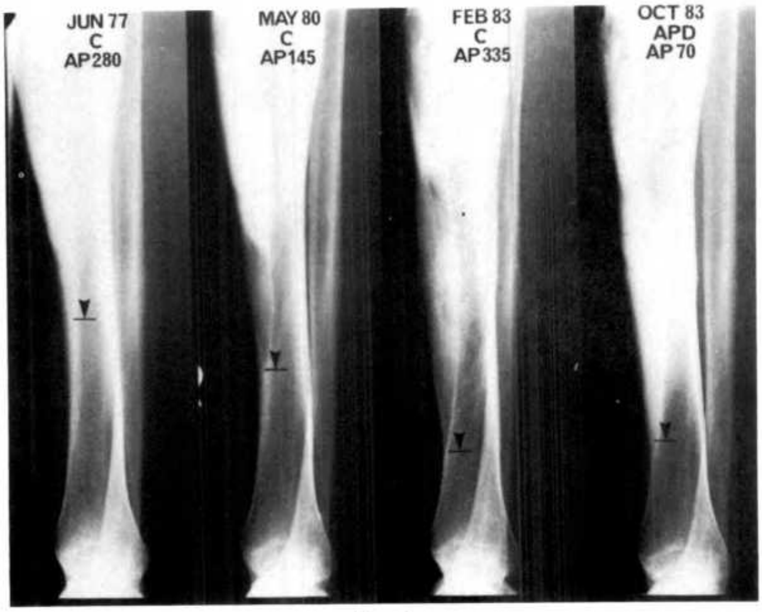


FIG. 6.

Downward progression of the lytic wedge between 1977 and 1983 with filling in of the lytic cortical area, wedge arrest, and apparent reversal in October 1983 at the end of a 6-month course of oral APD (10 mg/kg/day). The apparent fissure fracture halfway up the anterior border of the tibia in October 1983 is a film artefact. Note: suboptimal positioning in the radiograph of February 1983 makes estimation of the lower limit of the lytic wedge approximate only.

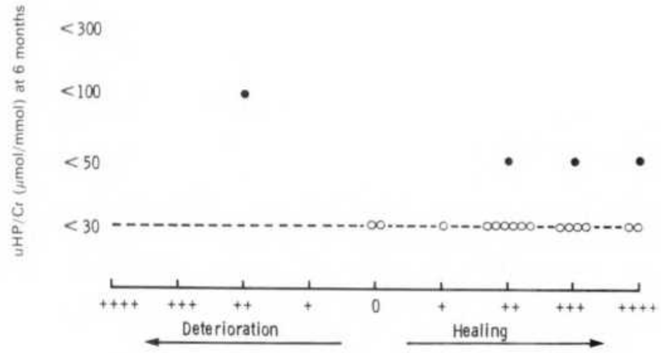


FIG. 7.

A comparison of the hydroxyproline/creatinine ratio and changes in 20 radiological lytic bone lesions 6 months after beginning a course of APD. The filled and open circles represent individual patients treated with intravenous and oral APD respectively. The method of assessment of radiological changes is described under Methods.

velocity in four patients with severe Paget's disease who had received successive courses of EHDP, calcitonin, EHDP plus calcitonin and APD over long periods.

*Case 1 (Fig. 9)*

This man, whose early medical history has been reported previously (Ooi et al, 1980), presented in 1965 with a lytic wedge lesion of the upper left tibia. Paget's disease was diagnosed on the basis of the radiological appearances and sAP of > 1000 IU/l. The finding of hypercalcaemia and an elevated serum parathyroid hormone level led to the subsequent diagnosis of primary hyperparathyroidism. Bone histology confirmed osteitis fibrosa and also showed evidence of Paget's disease. The removal of a parathyroid adenoma in early 1973 resulted in a fall in the serum calcium to normal, but no change in the serum alkaline phosphatase. Following parathyroidectomy there was a dramatic reduction in the tibial wedge velocity from 1.2 to 0.3 mm/month, with a temporary increase during a 6-month course of EHDP. Improvement continued with subsequent courses of combined EHDP plus calcitonin. Further rapid acceleration (0.6 mm/month) followed a period without treatment in 1981 until a 5-month course of oral APD in 1982 caused arrest and reversal of the

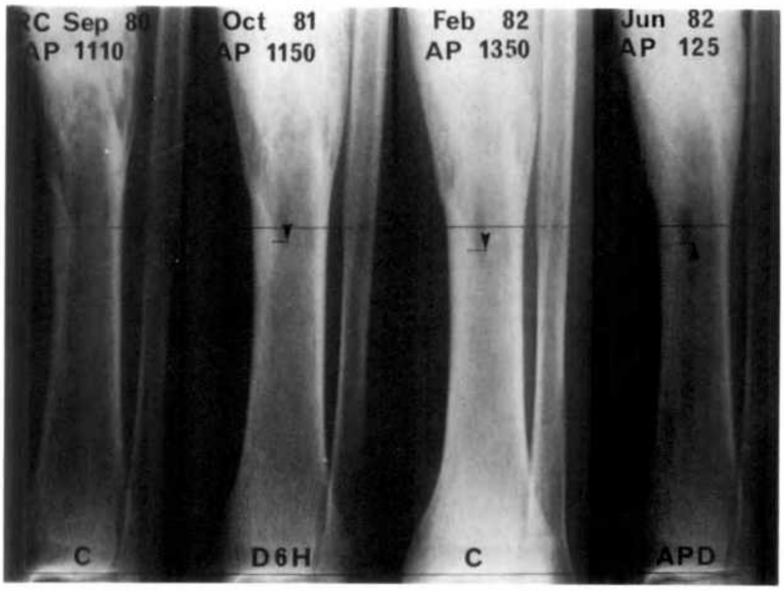


FIG. 8. *Case 1.*

Downward progression of lytic wedge between September 1980 and February 1982, despite a 6-month course of combined EHDP and calcitonin. Filling in of lytic cortical areas with wedge arrest and reversal at the end of a 5-month course of oral APD (10 mg/kg/day). Further slight progression occurred 6 months later.

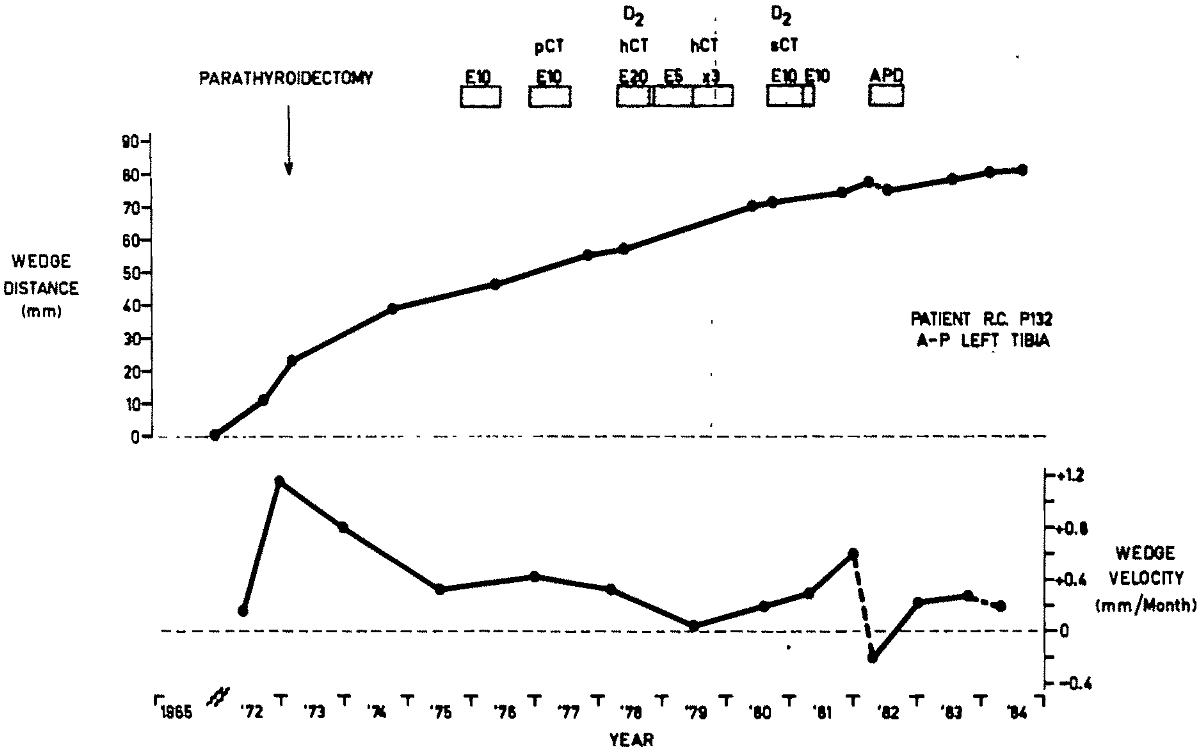


FIG 9. *Case 1.*

Changes in lytic wedge distance and velocity with successive therapies over extended periods Details are included in the text.

wedge progression (Fig. 9). Despite filling in of proximal osteolytic areas and full biochemical remission, there has been subsequent slight progression of the resorption front and further treatment is in progress

*Case 2 (Fig 10)*

This man presented with a lytic wedge in the right tibia in 1974 The sAP was then 550 IU/l. Following an initial course of oral EHDP (20 mg/kg/day) there was rapid progression of the lesion (wedge velocity = 0.6 mm/month) with radiological demineralisation and fracture in 1978. Fracture healing occurred following a 6-month course of calcitonin but the wedge continued to progress during subsequent courses of EHDP (5 mg/kg/day) and combined salmon calcitonin and EHDP (10 mg/kg/day) plus vitamin D Wedge progression was finally arrested and reversed following 6 months of oral APD 10 mg/kg/day in 1982, and the lytic area has since healed Biochemical indices remain normal 3 years after treatment

*Case 3 (Fig 11)*

This man received treatment with EHDP (10 mg/kg) for Paget's disease in 1976. Measurement of the tibial wedge showed slow progression (0 1 mm/month) during a subsequent course of combined calcitonin plus EHDP. In 1979, during a period without treatment there was a rapid increase in wedge velocity (2.7 mm/month) and this slowed again to 0 4 mm/month with combined therapy. A 6-month course of oral APD in 1982 resulted in biochemical remission and arrest and healing of the wedge. These results have been sustained until the present.

*Case 4 (Fig. 12)*

This man with severe Paget's disease and bilateral valgus deformity of both tibiae (sAP = 2850 IU/l) was first treated with EHDP in 1976 During successive courses of combined human calcitonin and EHDP in 1979, there was a reduction in wedge velocity to zero from an initial rate of 0.5 mm/month. There was subsequent reversal and regression of the wedge (−0.3 mm/month) during treatment with calcitonin alone and later vitamin D This improvement with calcitonin, which was sustained for longer than usual, continued during a 6-month course of oral APD with near biochemical remission and final wedge healing

## DISCUSSION

Both calcitonin (Bijvoet & Jansen, 1967) and the bisphosphonates EHDP and APD (Frijlink et al, 1979; Ibbertson et al, 1979; Fraser et al, 1984) have been shown to suppress biochemical indices of activity in Paget's disease This change is accompanied by a reduction in the concentration of bone-seeking radionuclides (Vellenga et al, 1976) and a fall in local blood flow and cardiac output (Henley et al, 1979). Bone histomorphometry of iliac crest biopsies shows reduction in osteoclast numbers and a return to the normal

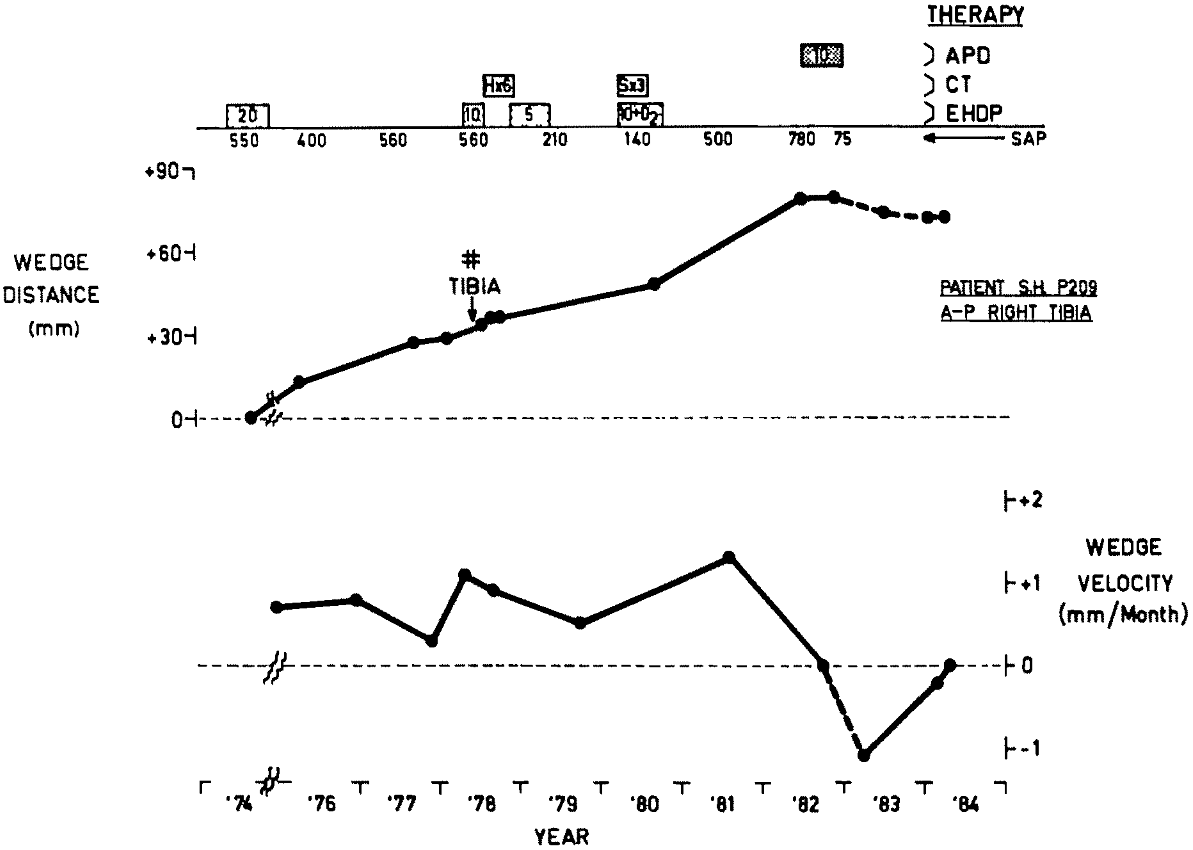


FIG. 10. *Case 2*

Changes in lytic wedge distance and velocity with successive therapies over extended periods. Details are included in the text.

lamellar arrangement of collagen fibres (Meunier et al, 1975; Yates et al, 1985). These various indices do not necessarily reflect structural changes in peripheral bone lesions, which may continue to progress and cause local pain and deformity. Bone radiology, on the other hand, allows a direct and clinically relevant assessment of changes in cortical and trabecular bone (Doyle et al, 1974). The common sclerotic radiological lesion of Paget's disease occasionally shows extension while under observation but this is rare, despite concurrent biochemical evidence of active disease. A reduction in the external diameter of expanded Pagetic bone has been demonstrated with calcitonin (Woodhouse et al, 1972), but exact positioning of matched radiographs is critical to such analysis and not easily achieved under routine conditions. In pure lytic lesions, bone turnover is rapid and changes with therapy detected more easily than in sclerotic bone. Although less common, such lesions are more easily measured, particularly in the skull and tibiae where reproducible positioning is more often possible. In the untreated patient, areas of cortical lysis in the skull and long bones may sometimes heal spontaneously. However, the apparent complete restoration to normal seen in the four skull radiographs of patients treated with EHDP and the consistency of healing of the linear cortical blade lesions within 6 months of a course of APD suggest a response to therapy. This is supported further by the arrest and healing of the lytic wedge lesions following APD, since without treatment these almost invariably progress (Nagant de Deuxchaisnes, 1977). The rate of progression of the resorption front gives a direct indication of the tempo of the disease process and correlates with clinical features such as pain, local heat and risk of fracture, but not always with biochemical indices of disease activity.

Using refined radiological techniques, calcitonin was shown by Nagant de Deuxchaisnes et al (1977) to induce bone healing in eight treated patients. The response was dose-dependent and occurred in spite of continued elevation of biochemical indices in some patients. The changes were reversed when calcitonin was stopped Others have reported similar results and spectacular healing of disseminated lytic Pagetic lesions

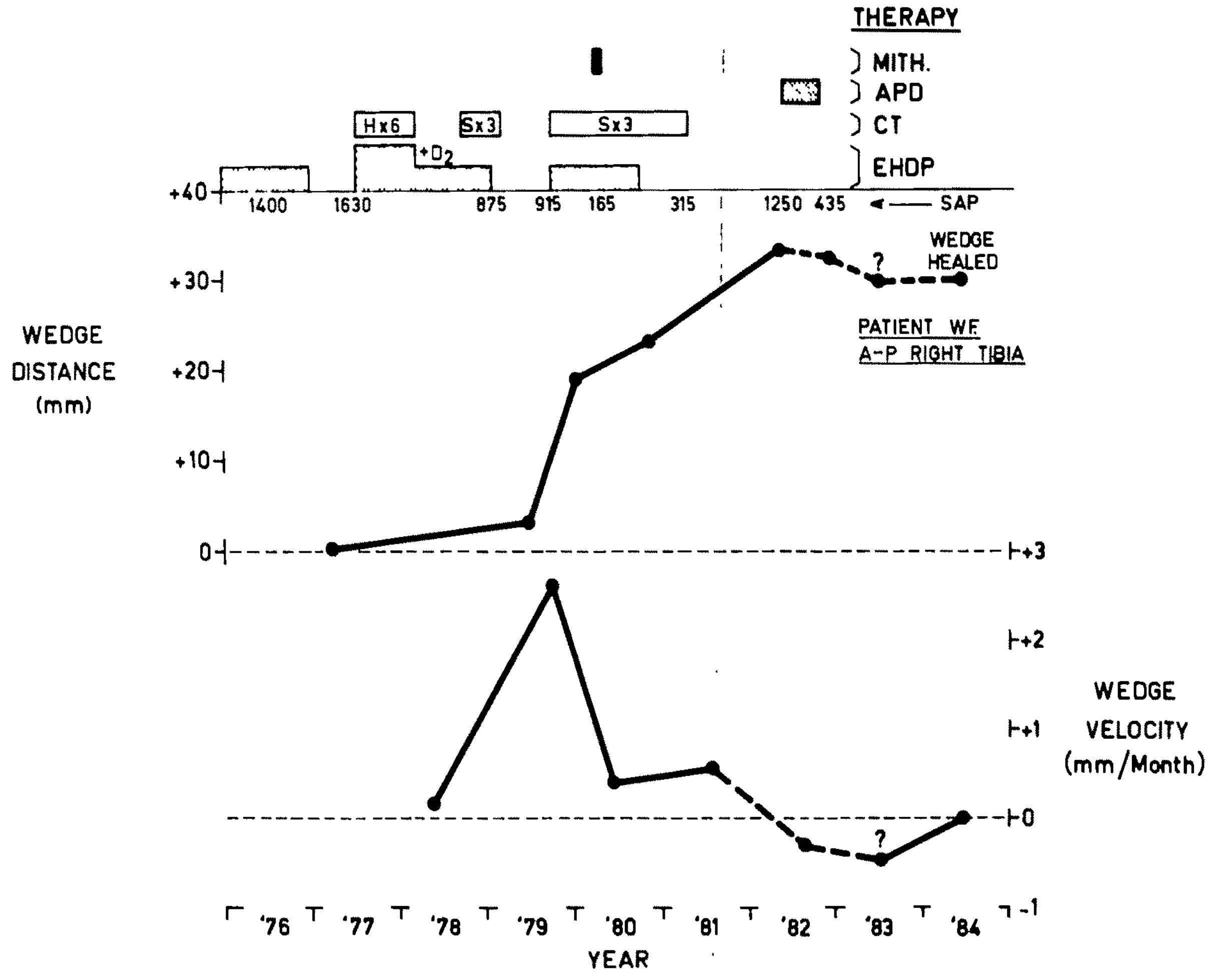


Fig 11. *Case 3.*

Changes in lytic wedge distance and velocity with successive therapies over extended periods. Details are included in the text.

was recently reported in a 28-year-old male (Whyte et al, 1985). The relief of bone pain and the high rate of biochemical remission with EHDP gave hope of sustained healing of bone lysis. Healing certainly occurs (Murphy et al, 1980) but was seen in only 20% of the patients treated with EHDP in the present study When it occurred, however, healing was sustained in all patients in whom the uHP/Cr ratio remained suppressed beyond 12 months Deterioration in bone texture was more usual, and occurred at dose levels of 10 and 20 mg/kg/day. These doses are higher than currently recommended but similar deterioration has been shown with doses as low as 5 mg/kg/day (Nagant de Deuxchaisnes et al, 1980). Occasional exacerbation of bone pain (Fromm et al, 1979) and histological evidence of focal osteomalacia (Boyce et al, 1984) have also been reported in patients receiving this dose. In a study of nine patients treated with EHDP (mean dose 7.0 mg/kg/day), Nagant de Deuxchaisnes et al (1981) reported the appearance of radiotranslucent lesions in five patients and dissociated "constructive and destructive" changes in a further four These varying effects probably reflect variability of absorption and local concentration of EHDP in active bone lesions. Aggravation of bone pain has in fact been noted more frequently in patients with single bone lesions in which the local concentration of the drug is likely to be higher (Fromm et al, 1979). Some protection is conferred by the addition of calcitonin (Nagant de Deuxchaisnes, 1979) and this combined therapy is accompanied by reduced evidence of osteomalacia (Bijvoet et al, 1980).

In contrast to the variable effects of EHDP, evidence of radiological healing was apparent in 17 out of 20 of our patients 6 months after beginning treatment with APD. In nine patients, cortical blade lesions all showed healing. Although treatment was not randomised, this

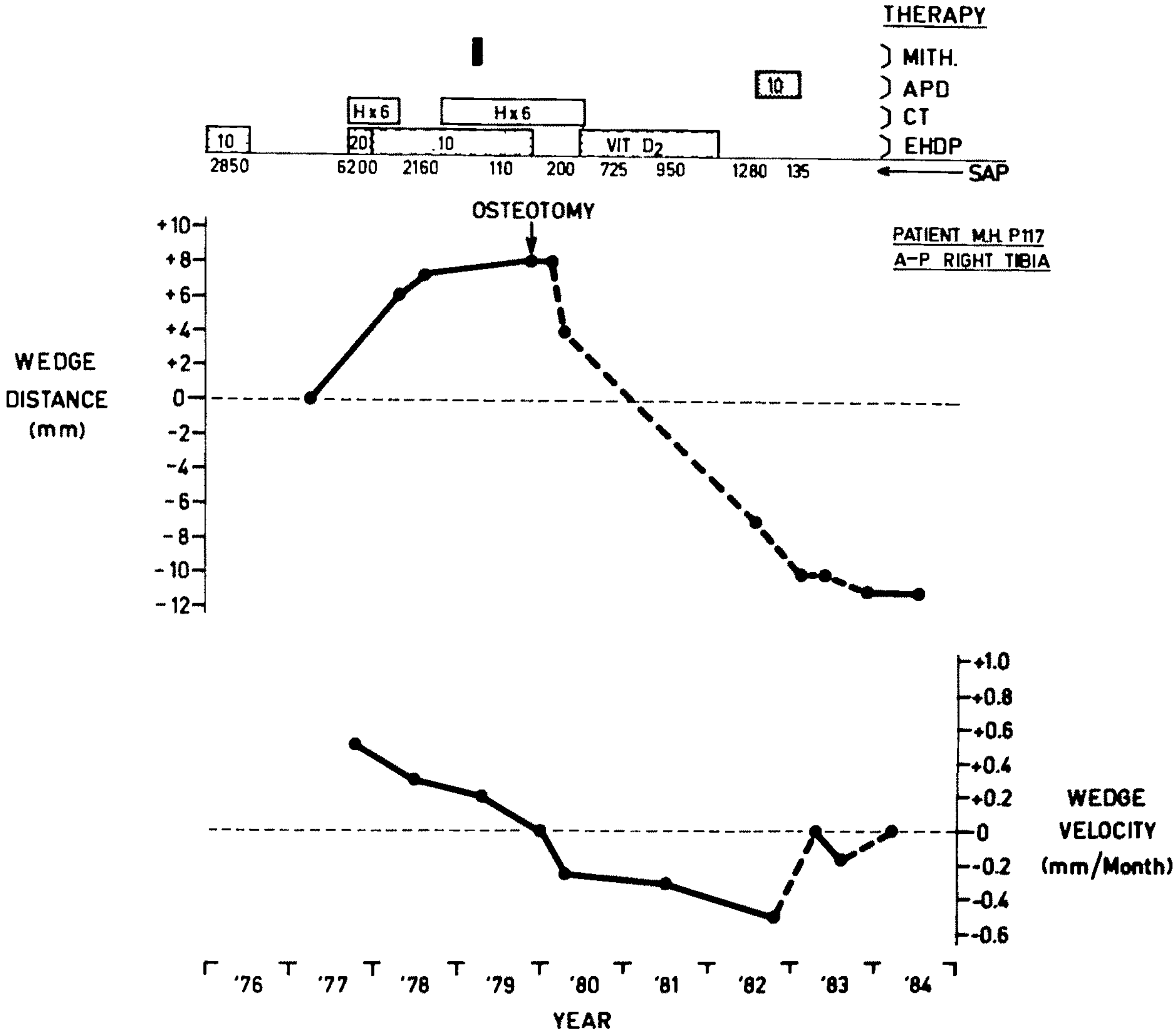


Fig. 12. *Case 4.*

Changes in lytic wedge distance and velocity with successive therapies over extended periods Details are included in the text.

stands in sharp contrast to the response of similar lesions treated with EHDP, when only 19% showed an improvement in bone texture. The changes observed at this time suggest that healing could have been detected earlier. Improvement in bone texture has in fact been reported in five out of nine patients as early as 2 months after beginning this drug (Nagant de Deuxchaisnes et al, 1982). In two of 17 patients reported by these authors the radiological appearance deteriorated and new lytic areas appeared during treatment with APD. Biochemical data were not reported. In one of our own patients with only a modest reduction in the uHP/Cr ratio, a wedge lesion continued to progress. This could indicate inadequate therapeutic effect, rather than a deleterious action of the drug. In this respect, APD differs from EHDP. Both drugs relieve bone pain and induce biochemical remission with similar frequency but radiological evidence of healing is almost the rule with APD and uncommon with EHDP. This difference reflects the relatively low potential for APD to interfere with bone mineralisation, as demonstrated in rat studies (Reitsma et al, 1980). The relationship between bone healing and biochemical response is of some interest. Although most patients in whom bone healing was observed during APD were in biochemical remission there were four in whom biochemical indices remained elevated. This differential effect is commonly observed during calcitonin therapy, cessation of which is usually followed by biochemical relapse and further deterioration in lytic lesions. Following APD, biochemical indices can remain suppressed for long periods and bone healing continued 12 months after beginning treatment in four out of five of our patients in biochemical remission. In one patient, however, in whom there was arrest and reversal of a lytic wedge at 6 months, further progression was observed at 12 months despite normal sAP and uHP/Cr. Thus, the achievement of biochemical remission does not guarantee continued healing of bone. This is perhaps not unexpected, since the contribution of a single lytic lesion to the elevation of biochemical indices may be quite small, particularly in patients with widespread disease. Continued elevation of skin temperature over the lesion which was apparent in this patient may, in fact, be a better indication of continued disease activity and the need for further therapy than biochemical measurements alone. Similar considerations apply to bone scintigrams, in which residual activity may reflect continuing disease activity despite normal biochemical tests. Although APD causes healing of the lytic process in Paget's disease, it cannot be assumed that this will be accompanied by changes in the osteosclerotic bone lesions in which excessive and disorderly bone formation predominates. However, the reduction in activity shown by bone scintigraphy and the reversal of histological changes in iliac crest biopsies suggest that remodelling is also taking place in this type of lesion. To confirm this it will be necessary to follow carefully matched radiographs over long periods.

### ACKNOWLEDGMENTS

The authors wish to acknowledge the generous gift of APD from Professor O. L. M. Bijvoet and the expert secretarial assistance of Mrs Eileen Bambury. The research was supported by the New Zealand Medical Research Council.

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# Book review

*Radiologic Management of Musculoskeletal Tumors.* By Holger Pettersson, Dempsey S Springfield and William F. Enneking, pp xi+153, 1987 (Springer-Verlag, London), £62.00
ISBN 3-540-16756-0 (Berlin)
0-387-16756-0 (New York)

During the last 15 years, advances in surgical technique and biomedical engineering have changed the approach to tumours of the appendicular skeleton to one of limb preservation with prosthetic replacement. In addition to this, in the last 5 years or so, the use of pre-operative chemotherapy, under the careful control of experienced oncologists, has often meant that neoplasms, previously considered unsuitable for conservative surgery, have been treated successfully by prosthetic replacement. The management of musculoskeletal tumours is a matter of teamwork and the altered approach to treatment has produced new stimulation as well as new problems for the radiologist. This small book, from a leading centre in the United States, aims to provide a concise discussion of the pre-operative radiological investigation, not only for those in tumour centres but also, perhaps more importantly, for referring centres, where such patients are encountered only infrequently

The book begins with general pathological principles Although the preface stresses the need for teamwork, none of the authors is a pathologist; the quality of the pathological discussion is poor and the text soon moves on to the authors' well publicised staging system. A strong differentiation is made between malignancy, benignancy and local behaviour believing that, in the planning of definitive surgery, the histopathological diagnosis is less important than the local behaviour and extent of the tumour as evaluated radiologically. Hence, the terms "latent", "active" and "aggressive" are used in assessment

Basic radiological diagnosis, during almost the last 20 years in this field, has rightly rested on Lodwick's radiological grading of tumoral growth rate. The case for such simplification as is given in this book is, to say the least, unconvincing.

All the imaging modalities are assessed in separate chapters covering both technical matters and diagnostic value. Although most of this material could be found in any standard radiological text, it is convenient for it to be grouped together for the reader interested only in musculoskeletal tumours. The continuing supremacy of the plain radiograph in initial radiological diagnosis is acknowledged, as is the unique contribution of skeletal scintigraphy in determining the activity and vascularity of a lesion, on several occasions "nucleotide" is used erroneously, when "nuclide" is intended. The technical use of angiography is well discussed in a short section by Irvin Hawkins, but the limited capability of the technique in diagnosis and assessment of local neoplastic behaviour is admitted elsewhere in the text It may be impossible to determine with computed tomography whether a plane of normal tissue exists between the tumour and the neurovascular bundle, in the popliteal fossa, arteriography with the knee in flexion is advocated in dealing with this problem Not all the opinions are of course non-controversial, as William Hazlitt said, "When a thing ceases to be a subject of controversy, it ceases to be a subject of interest" The arguments are, however, reasoned and balanced. The occasional phrase seems problematical, "the periosteal expanded shell is merely the expanded cortical capsule around an active lesion" sounds profound, but on reflection is virtually meaningless. A penultimate chapter usefully records the authors' work on the relative values of the different imaging methods which, *inter alia,* confirms the overall unique value of magnetic resonance imaging in the elucidation of the tumours of soft tissues and bony neoplasms with major soft-tissue involvement The book ends with nine illustrative cases in which the practices propounded are followed and a surgical stage denoted.

If there was anything I missed in this book, it was the lack of the true quintessence of a bone tumour unit This may be because the authors' bias is to a surgical view of radiology, despite the title, two of the three authors are surgeons and the third is a distinguished visiting professor of radiology. The dialogue of a working relationship somehow does not emerge from these pages. Bone tumour work is a corporate business, but at the time of diagnosis, it has to be said, the involvement of the surgeon is minimal, except as the leader of the team The dialogue at this stage is between the radiologist and the histopathologist and this is missing in this work.

The book is well laid out, with excellent illustrations, it was interesting to find that this distinguished German publishing house had used a British printer

I consider this a first-class short presentation of the subject, which will prove of most value to the orthopaedic surgeon and radiologist who occasionally have to deal with a bone tumour and refer the patient to a major centre. it is well produced, but somewhat expensive for a review of an ever-changing topic.

DENNIS STOKER

1987, *The British Journal of Radiology*, *60*, 861–864 SEPTEMBER 1987

# Measurement of relative renal function. A comparison of methods and assessment of reproducibility

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*(Received May 1985 and in revised form December 1986)*

## ABSTRACT

A good correlation was found between relative uptake of $^{99}Tc^{m}$ dimercaptosuccinic acid (DMSA) and relative $^{131}I$ orthoiodohippuric acid clearance in a group of 100 consecutive patients without evidence of renal failure. In the majority, attenuation correction was found to make no significant difference to relative function measurement. Those in whom it did could be readily identified by inspection of the posterior DMSA images at the time of examination. Two hundred patients were reviewed in whom serial studies had been performed over the previous 5 years Differences in relative function greater than 5% indicated a high probability that a real change in renal function had occurred We conclude that whilst renography and DMSA scintigraphy yield complementary information, relative function (L/L+R) can be measured equally well by either method, and the results are sufficiently reproducible to be clinically useful.

A number of non-invasive techniques have been described for estimating the separate contribution of each kidney to total renal function. Most employ radioactive tracers. The parameter measured may be described as functioning cortical mass (Kawamura et al, 1978), relative blood flow (Daly et al, 1979) or relative glomerular filtration rate (Dubovski & Russell, 1982). Tracer techniques validated against standard reference and invasive methods include uptake of mercuric chloride (Raynaud, 1974), chloromeradrin (Secker-Walker & Coleman, 1976), $^{99}Tc^{m}$ dimercaptosuccinic acid (DMSA) (Daly et al, 1978; Kawamura et al, 1978; Taylor, 1980) and clearance of orthoiodohippuric acid (OIH) labelled with $^{131}I$ or $^{123}I$ (Hayes et al, 1974; Shames & Korobkin, 1976).

A good correlation has been found between DMSA uptake and OIH clearance in subjects with serum creatinine concentrations of less than 20 mg/l (Taylor, 1980; Daly & Henry, 1981) but not in the presence of raised serum creatinine level or of outflow obstruction (Taylor, 1982). No reports on the reproducibility of relative uptake measurements have appeared since the original description by Raynaud (1974) using $^{197}HgCl_2$.

In reviewing the relative uptake of $^{99}Tc^{m}$ DMSA over a period of 5 years it became evident that some of the variability may be due to changes in renal depth. Although the variable effect of posture on renal position, renal depth and observed count rate has been documented (Nimmon et al, 1975; Daly et al, 1978), not all of the published comparisons indicate whether or not any correction was made for differences in renal depth. Some do not indicate the posture of the patient during the measurement (Kawamura et al, 1978) The fact that a good correlation may be found, even without this correction, indicates that it may not be of importance in the majority of patients. However, we have observed some patients in whom there is a large difference between corrected and uncorrected values. It would therefore be useful if the conditions under which depth correction is required could be defined.

We have compared the relative uptake of $^{99}Tc^{m}$ DMSA and $^{131}I$ OIH clearance simultaneously in 100 patients. As both depend on tubular rather than glomerular function the results ought to be related. We also reviewed 200 patients in whom relative function was measured on more than one occasion, to ascertain the reproducibility of the method over a long period and the clinical significance of a difference between values obtained on different occasions.

## METHODS

To study the reproducibility of $^{99}Tc^{m}$ DMSA relative function (L/L+R) measurements, 214 patients who had had more than one examination with this preparation in the last 5 years were identified from the department records and their notes and subsequent follow-up reviewed. Nine were excluded because of inadequate clinical information on follow-up and another five were excluded because they were in renal failure at the time of one or both examinations. The study therefore consists of 575 examinations in 200 patients.

A dose of 70 MBq $^{99}Tc^{m}$ DMSA (proportionately lower in children) was administered intravenously. In adults $^{131}I$ OIH renography was performed with a gamma camera equipped with a very sensitive high-energy collimator, starting 10–15 min after administration of DMSA, which was used for accurate positioning and subsequent imaging and relative uptake measurement. With the pulse-height analyser of the gamma camera set to the $^{131}I$ window, no counts from the $^{99}Tc^{m}$ could be detected. Two megabecquerels of $^{131}I$ OIH was administered intravenously, immediately

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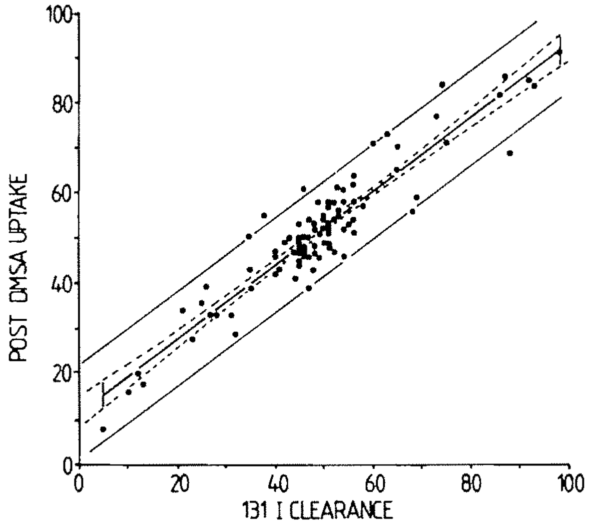

Fig. 1

Relative OIH clearance plotted against DMSA uptake, single posterior erect view, $n=100$, $r=0.93$, $y=0.82x+11$ (95% confidence limits shown).

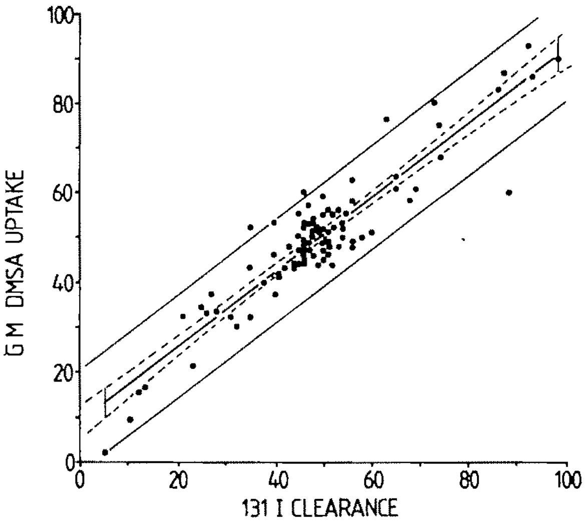

Fig. 2.

Relative OIH clearance plotted against geometric mean (GM) DMSA uptake; $n=100$, $r=0.922$, $y=0.84x+8.5$ (95% confidence limits shown)

followed by 2 mg of bumetanide. This ensured the examinations were carried out under conditions of maximal diuresis. Counts were collected at a rate of 4 frames per min for the first 5 min, then 2 frames per min for a further 25 min. Relative function was calculated by measuring the area under the background-subtracted curve for each kidney from 45 to 135 s after the arrival of tracer at the kidneys (Britton, 1975). This part of the study was performed with the patient supine to minimise the risk of hypotension following bumetanide and to minimise the effect of nephroptosis.

The relative uptake of DMSA was estimated using a single posterior erect view, after subtraction of background estimated from the region between the kidneys.

In order to ascertain the significance of a difference in relative uptake on two occasions, case notes were reviewed to determine what pathological process, if any, could account for an observed change, for example relief of obstruction, heminephrectomy or a clear change in radiological or scintigraphic appearances.

A second group of 100 consecutive patients was observed to study the effect of depth correction on relative function calculations using DMSA. Here, the relative uptake calculated from a posterior erect view was compared with that derived from the geometric mean of the counts in both posterior and anterior erect views. In each patient, relative function was also estimated using $^{131}$I OIH as described above, to observe the correlation between these techniques.

## Results

Relative OIH clearance (supine) is plotted against DMSA uptake (single posterior erect view) in Fig. 1. Figure 2 demonstrates OIH clearance plotted against geometric mean DMSA uptake. Figure 3 shows posterior against geometric mean uptake of DMSA. Table I contains the mean absolute differences between pairs of measurement methods of relative function, with

TABLE I

Mean absolute differences between pairs of measurement methods

| Methods | Mean absolute difference | Standard deviation | Standard error | *n* |
|---|---|---|---|---|
| OIH clearance<br>posterior DMSA | 3.05 | 3.94 | 0.39 | 100 |
| OIH clearance<br>GM DMSA | 3.15 | 4.27 | 0.42 | 100 |
| Posterior DMSA<br>GM DMSA | 3.01 | 3.91 | 0.39 | 100 |

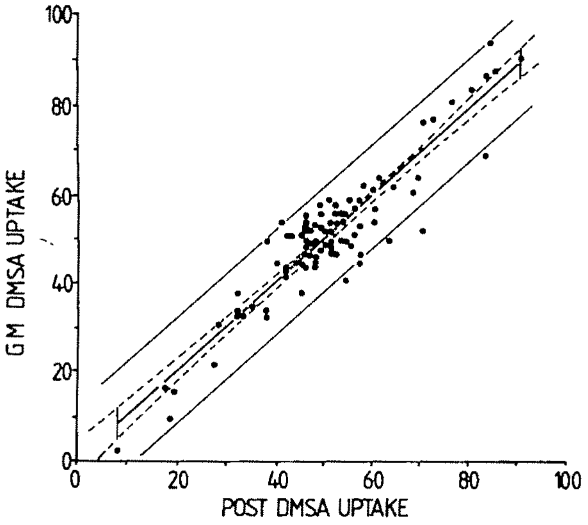

FIG. 3.

Posterior uptake plotted against geometric mean (GM) DMSA relative uptake; $n=100$, $r=0.922$, $y=0.97x+2.4$ (95% confidence limits shown).

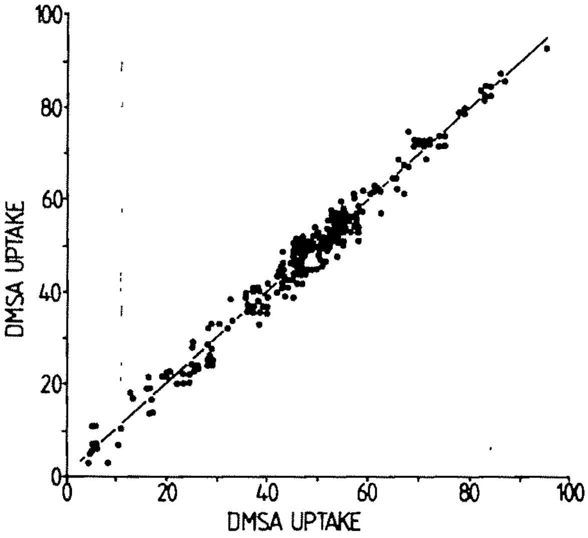

FIG 4.

Relative DMSA uptake on different occasions with no reason to expect real change; $n=359$, $r=0.987$, $y=0.99x+0.36$.

their standard deviations and standard errors. In all these comparisons the data were obtained during the same examination session For follow-up studies, only posterior DMSA uptakes were considered, as the majority did not have a geometric mean measurement.

Figure 4 illustrates the correlation between DMSA relative uptake in 200 patients seen more than once, with a total of 359 pairs of examinations These patients constituted Group 1, in which there was no evidence to suggest that a change in relative function had occurred between examinations. Figure 5 shows the same group with Group 2, in which there were reasonable grounds to expect real change

## DISCUSSION

The results in Figs 1–3 and Table I show that relative function measured by OIH clearance and DMSA uptake have a high degree of correlation and are therefore almost certainly measuring the same or intimately related parameters. It has been suggested that DMSA is bound to the metal-binding protein metallothionein, found in the cytosol and mitochondria of proximal tubular cells (Boyd, personal communication). The uptake of DMSA is therefore likely to be an index of functioning proximal tubular mass. The clearance of OIH is by secretion, principally from the proximal tubules. It is clear from our results that in most cases relative function can be measured equally well using DMSA uptake or OIH clearance, even though they may represent different metabolic activities of the same cells.

In some cases a large difference was observed between relative DMSA uptake (single posterior erect view), geometric mean relative DMSA uptake and OIH clearance (posterior, supine). We have reviewed the DMSA images and a summed view of the 30 min OIH renogram in 100 cases. In 70 of these patients, in whom the upper poles of the kidneys were within one half of one kidney length of each other on the posterior DMSA image and in whom the kidneys did not appear rotated, differences between the relative function measured by the two methods were less than 5%. Thus, an attenuation correction is unnecessary for measurement of relative function in the majority of patients. A difference of greater than 5% in relative uptake between the supine (measured with OIH) and erect position (measured with DMSA) was present in 30 patients.

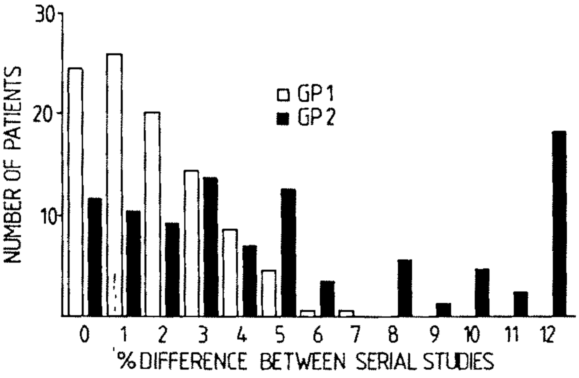

Fig 5.

Percentage change between different occasions in Group 1 (with no reason to expect real change) (open bars) and Group 2 (with good reason to expect real change) (solid bars)

Mobility of one or other kidney accounted for the difference in the majority. In these patients a supine posterior view is preferable to an erect view for calculation of relative function, and is as good as the geometric mean of the anterior and posterior erect views. Only in seven was there a fixed rotation. An anterior DMSA view for depth correction using the calculated geometric mean count rate (Pettit et al, 1971) needs to be acquired only in this latter group. In a small number of patients we have observed a large discrepancy between DMSA and OIH which cannot be accounted for by purely technical factors At the present time we have no satisfactory explanation for this observation.

Three groups of patients emerged from the follow-up studies:

1 those in whom there was no reason to believe that any change in renal function had occurred;
2 those in whom there were reasonable grounds to expect a change;
3 those whose scintigraphic appearances suggested a change in positioning such as obliquity to the camera on one or other of the examinations. These were mostly patients with a severe kyphoscoliosis, in whom accurate repositioning was not possible.

The third group was excluded from further analysis. Patients with chronic obstruction, reflux or intercurrent infection were not included in Group 1. This study therefore gives a low estimate of the incidence of real change in renal function. When patients had been examined on more than two occasions the difference between every possible pair of results was considered.

By application of Bayes' theorem to the frequency distributions in Fig 5, it is evident that there is no cut-off point below which a difference in relative DMSA uptake is proof that no real change of differential function has occurred However, a change in relative function of greater than 5% indicates a high probability ($p = 0\,05$) that it has. The larger the difference, the greater the probability that the change is real. Together with biochemical measurement of absolute function, this is a useful indicator of progression of renal disease.

## CONCLUSIONS

Relative renal function can be measured equally well in most cases using $^{99}$Tc$^{m}$ DMSA or $^{131}$I OIH, the supine projection being preferable to the erect.

It is not necessary routinely to make attenuation correction, unless the upper border of one kidney is below the mid-point of the other, thus saving camera and processing time

The routine measurement of relative function enhances the value of both OIH renography and DMSA scintigraphy, especially when follow-up studies are contemplated.

ACKNOWLEDGMENTS

The authors express their thanks to Kate Ritchie (Superintendent Radiographer) and her colleagues, without whose willing assistance this study would not have been possible, and to George S. Boyd, Professor of Biochemistry, Edinburgh University, who sadly died in 1983, for valuable discussions on the mechanism of DMSA binding.

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1987, *The British Journal of Radiology*, 60, 865–868 SEPTEMBER 1987

# The renal parenchymal junctional line in children: ultrasonic frequency and appearances

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(*Received January 1987*)

ABSTRACT

The kidneys of 72 children were examined ultrasonically to determine the frequency of visualisation of the parenchymal junctional line (PJL), its variation with age and its ultrasonic appearances. The PJL was seen in 47 cases, usually on the right side. No statistical variation in the frequency of visualisation with age has been established. The usual appearance is of a thin, echogenic, linear structure running from the renal sinus to the cortex in an antero-superior direction. It is believed to originate from a layer of connective tissue which is trapped when a proportion of kidneys form from the fusion of two metanephric elements. The PJL is a common ultrasonic finding in a normal child's kidney and should never be confused with a pyelonephritic scar.

Following recent reports (Carter et al, 1985; Hoffer et al, 1985) of the ultrasonic observation of an echogenic defect in the kidneys of both adults and children, we wish to confirm the identification of such a structure, the parenchymal junctional line (PJL) in our own paediatric population. The structure we refer to as the PJL has been subdivided by Hoffer et al (1985) into a triangular perirenal, echogenic focus on the cortical surface of the kidney, the so-called parenchymal junctional defect (PJD) and the intraparenchymal linear echogenic component referred to as the inter-renicular septum.

The purpose of the study was to record the incidence of and the effect of age on the ultrasonic identification of the PJL in our paediatric population. The ultrasound appearances are presented and their nature discussed.

## MATERIAL AND METHODS

Over a 4-month period, 72 children (32 male and 40 female) between the ages of 1 month and 15 years were examined prospectively by the authors. In addition to the ultrasound examination as dictated by the clinical problem (usually urinary tract infection), a careful search was performed for the PJL bilaterally in anterior, anterior oblique and posterior projections in both longitudinal and transverse planes. A Diasonics DRF 400 real-time ultrasound machine, with both 5 MHz and 6.5 MHz mechanical sector probes, was used in all cases. Occasionally this was supplemented by an Emisonic mechanical B-mode scanner with 5 MHz or 7.5 MHz probes.

Children in whom renal disease was shown on either side or where good visualisation of both kidneys was not obtained were excluded from the study.

For a positive result to be recorded, an echogenic line and/or wedge had to be clearly identified extending from the cortical surface of the kidney to intersect the echo complex of the central sinus. Cases in which there was doubt were recorded as negative.

## RESULTS

Of 72 patients examined, a PJL could be identified in one or both kidneys in 47. On anterior (supine) scans, 44 were on the right side and eight on the left. On posterior (prone) scans, one each was on the right and left.

Figure 1 demonstrates the usual appearances of the PJL seen from the anterior oblique aspect in longitudinal section. A narrow straight echogenic line is seen passing from the renal sinus antero-superiorly to the renal cortex. Occasionally, a curved rather than straight line may be seen (Fig. 2). The superficial aspect

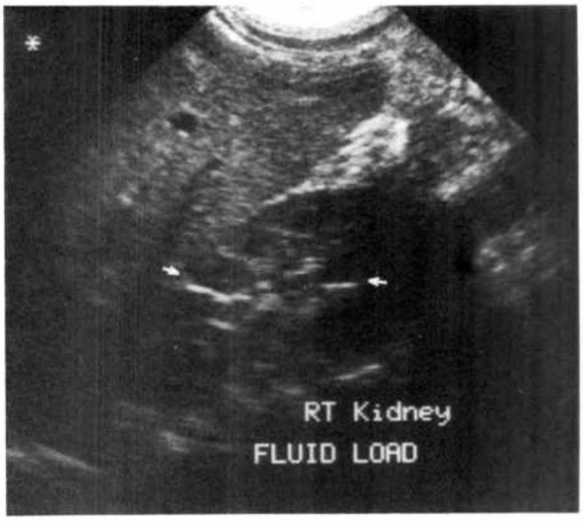

FIG. 1.

Right kidney, longitudinal section from antero-laterally. The junctional line is seen in both upper and lower poles (arrows).

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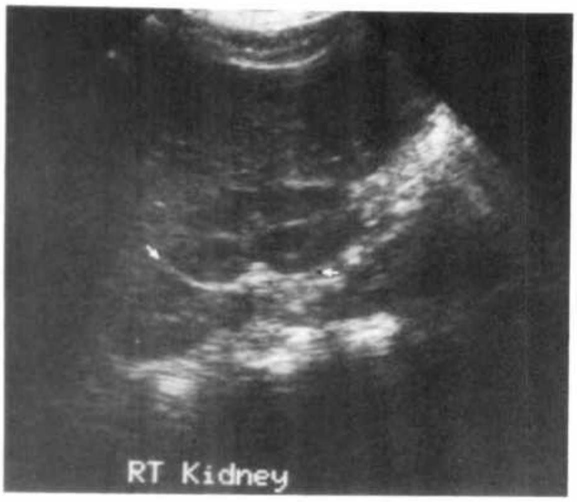


FIG. 2.

Right kidney, longitudinal section from antero-laterally. The junctional line is seen as a curved structure (arrows).

of the PJL may appear as a small echogenic triangle or wedge on the anterior surface of the kidney (Fig. 3). In transverse section, the PJL is seen running in the coronal plain in the anterior cortex of the upper pole (Fig. 4). When visualised in the lower pole, the PJL has the same orientation as in the upper pole, *i.e.* running anteriorly and superiorly (Fig. 5). The appearances on the left side are similar (Fig. 6).

The distribution of results according to age is shown in Fig. 7. Analysis by the $\chi^2$ test indicates that the differences between the age distribution and negative observations is not statistically significant ($0.50 > p > 0.10$).

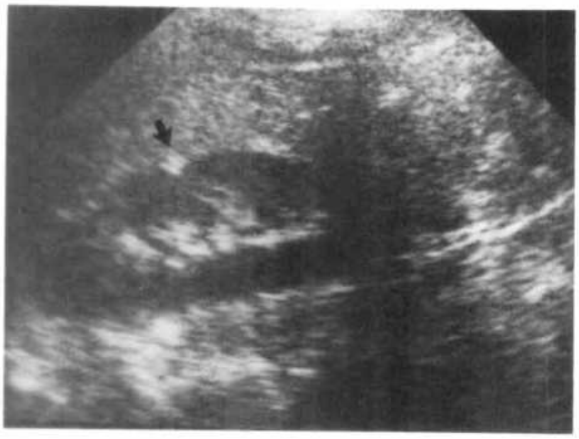
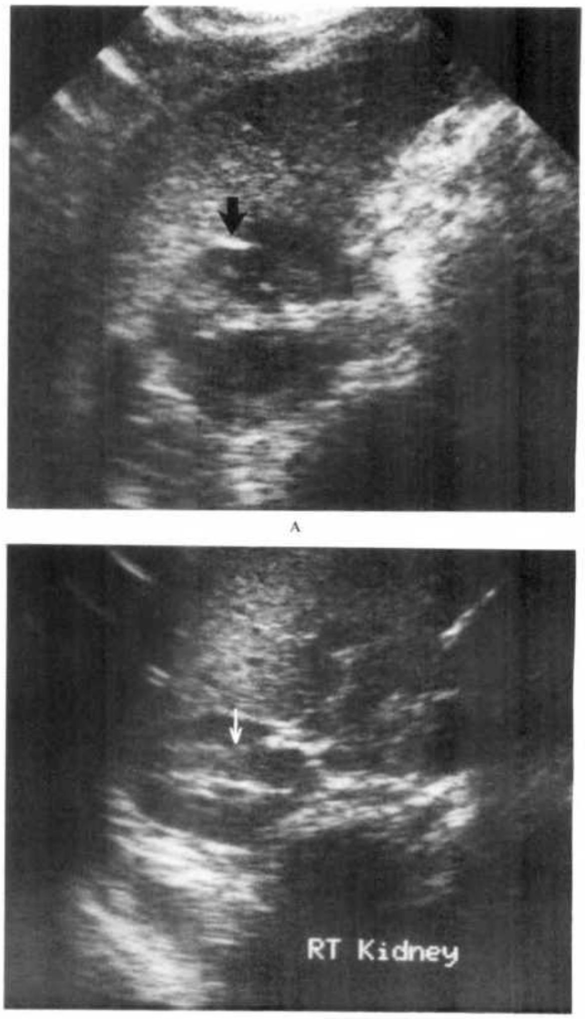


FIG. 3.

Right kidney, longitudinal section from anterolaterally. A portion of the junctional line is seen as an echogenic wedge (arrows).



A

B

FIG. 4.

(A) and (B) right kidney, from anterior. Two examples of the junctional line (arrows) seen in transverse section in the upper pole.

## DISCUSSION

From the figures it is clear that the PJL is most often visualised in the upper pole of the right kidney and is observed less frequently in the lower pole. The distribution is similar to that described by other authors (Carter et al, 1985; Hoffer et al, 1985). We found the most successful approach to be from the antero-lateral aspect, with the patient in the right anterior oblique position. This allows best use of the liver as an acoustic window. Visualisation of the PJL from the posterior aspect is uncommon. This may be because scanning perpendicular to its oblique plane is prevented by the spine.

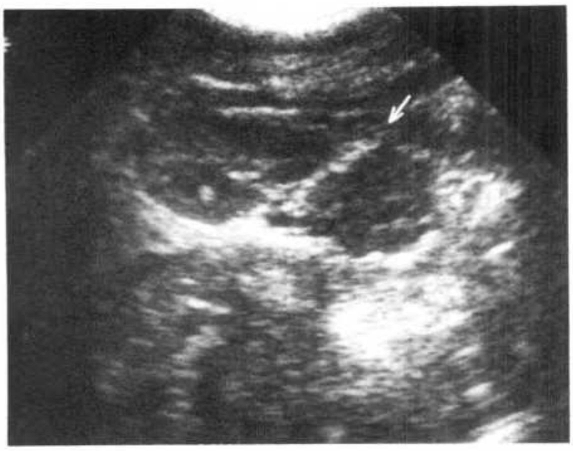


FIG. 5.

Right kidney, in longitudinal section from posterior, junctional line seen in the lower pole (arrows).

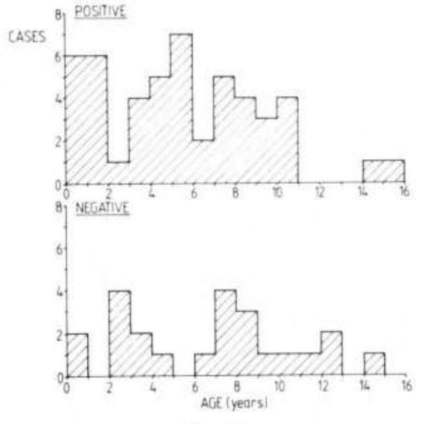


FIG. 7.

Distribution of positives and negatives with age.

In this series we were unable to prove decreasing visualisation with advancing age. Despite this, it is our impression that the PJL is seen less frequently in the adult population.

Unfortunately, the study by Carter et al (1985) fails to give figures for either negative or total examinations, making it impossible to judge the proportion of positives. Our own figures are, however, comparable with those of Hoffer et al (1985).

What is the nature of the PJL? The lobe is the basic unit of structure of the kidney. Each of the 14 or so lobes is roughly hemispherical, consisting of a central papilla and its surrounding cortex. The cortex of adjacent lobes extends into the centre of the kidney as a column of Berlin. Since there is no connective tissue between the two layers of cortex in the column of Bertin, the PJL echoes cannot originate here. Brodel (1901) describes a longitudinal depression on the lateral border of the kidney along which the capsule may be thickened and the perirenal fat more adherent than elsewhere. This line overlies the column of Bertin between the anterior and posterior calyceal rows and is purely a surface feature. It runs supero-inferiorly with no oblique sagittal inclination. The PJL is clearly quite a different structure from Brodel's white line.

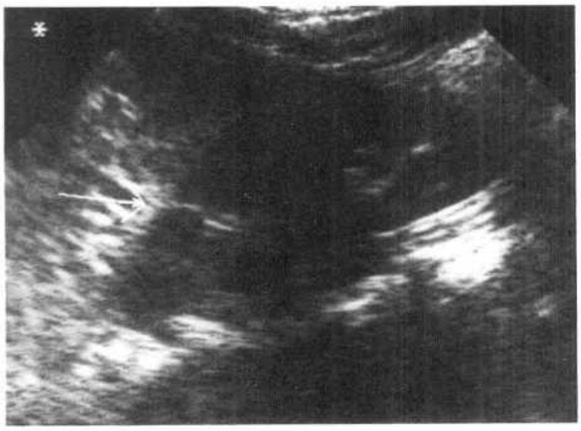


FIG. 6.

Left Kidney, longitudinal section from antero-laterally. Junctional line in the upper pole (arrow).

We agree with Carter et al (1985) and Hoffer et al (1985) that the answer lies at a more fundamental embryological level. The kidney parenchyma develops from a group of cells low on the urogenital ridge of the embryo, the metanephrogenic tissue or metanephros. The early metanephros consists of two layers. A loose, outer layer becomes the capsule and interstitial connective tissue of the kidney, while inner cells are destined to become the nephrons (Potter, 1972; Arey, 1974). The ureteric bud, arising from the lower end of the pronephric duct, indents the metanephros and divides to form the collecting system.

It has been reported that in five embryos examined the kidney developed by fusion of two parenchymatous masses (Fine & Keen, 1966). It was noted that the lower mass overlaps the upper anterior and the authors infer correlation between this observation and the finding of an intermediate cortex running obliquely, through the kidney from inferiorly, upwards and anteriorly, in kidneys where the collecting system splits predominantly into upper and lower major calyceal groups (75 of 107).

Radiological confirmation of a two-piece kidney was made by Dalla Palma and Rossi (1982), who demonstrated tomographically two distinct "renunculi" in 76 of 176 kidneys. The upper renunculus forms the superior and much of the posterior aspect of the kidney while the lower renunculus forms the inferior pole and most of the anterior aspect of the kidney.

There seems, then, good evidence that the kidney, at least in some of the population, results from the fusion of two renunculi. This is perhaps not surprising if one considers the segmental nature of the other primitive kidneys, the pro- and mesonephros and the frequent multiplicity of renal arteries. The PJL therefore represents the outer layer of the two metanephric elements which, upon fusion, gives rise to a plane of connective tissue running upwards and anteriorly through the kidney.

The significantly different ultrasonic incidence of the PJL on each side was partially explained by Dalla Palma et al (1982), who identified an interface between two renunculi in 57% of kidneys on the right side against 29% on the left. They also assessed the obliquity of the interface and noted that there was a considerable difference in the incidence of marked obliquity of the interface, being 42% on the right side and 16% on the left. We also speculate that the greater discrepancy in ultrasonic detection of the PJL between the two sides is, in part, related to the difficulty in obtaining suitably angled anterior oblique scans of the left kidney in the absence of an acoustic window comparable with the liver on the right side.

The PJL is clearly a normal anatomical structure. It is not associated with focal loss of parenchyma and should never be confused with a pyelonephritic scar.

ACKNOWLEDGMENTS

The authors wish to acknowledge the patient and efficient secretarial assistance of Miss Jennifer Anderson.

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1987, *The British Journal of Radiology*, 60, 869–872 SEPTEMBER 1987

# The importance of using anterior and posterior views in the calculation of differential renal function using $^{99}$Tc$^{m}$-DMSA

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*(Received August 1986 and in revised form December 1986)*

ABSTRACT

Radionuclide techniques for determining relative renal function are well established. One simple method uses the count rate from static images obtained using $^{99}$Tc$^{m}$-dimercaptosuccinic acid (DMSA). We have reviewed 277 DMSA scans and shown that it is important to obtain the geometric mean of counts from the anterior and posterior views in order to correct for the different amounts of attenuation for each kidney. If counts were obtained from the posterior view only, erroneous results would be obtained in 8% of children under 13 years, in 28% of patients aged between 13 and 20 years and in 32% of patients over 20 years of age.

Accurate determination of individual renal function requires ureteric catheterisation to assess clearance from each kidney. This technique is not only invasive, but is also time consuming and requires surgical expertise to perform. Using radionuclide techniques it is possible to assess differential renal function quite simply and non-invasively. If a dynamic renal study is performed with either $^{123}$I-hippuran or $^{99}$Tc$^{m}$-DTPA, the relative renal function may be calculated from the ratio of the background-corrected count rate from each kidney between 1 min and 3 min (O'Reilly et al, 1986). Alternatively, the relative renal function may be determined from static images taken a few hours after administration of an agent, such as $^{99}$Tc$^{m}$-DMSA, which is largely bound in the kidney. In the absence of any obstruction, the determination of differential renal function using $^{99}$Tc$^{m}$-DMSA produces results comparable with those from a dynamic study (Bingham & Maisey, 1978). While studies involving ureteric catheterisation have shown that DMSA uptake correlates well with the individual glomerular filtration rate and creatinine clearance (Born et al; 1978, Daly et al, 1979; Powers et al, 1981), there are two different methods of obtaining the renal count rate. Some authors have reported results obtained from the posterior counts only (Price et al, 1979; Peters et al, 1986) while others have taken the geometric mean of the counts from the anterior and the posterior views (Taylor, 1982; Wujanto et al, 1986). If the right and left kidneys lie at different distances from the camera, then the ratio of the count rates will not reflect the true relative function because of the different amounts of gamma-ray attenuation. Taking the geometric mean of anterior and posterior count rates provides an approximate correction for this effect. The purpose of this study was to investigate whether the difference between the results obtained using the geometric mean and those obtained using the posterior counts only was sufficient to warrant using the more complicated technique in all patients.

## PATIENTS AND METHODS

All DMSA scans performed in the last 4 years were studied retrospectively and the relative renal function noted. Patients with a solitary kidney were excluded from the study. The scans were performed 2–3 h after an injection of 1 MBq/kg body weight of $^{99}$Tc$^{m}$-DMSA. Static images (duration 5 min) were acquired on a 128 × 128 matrix using a gamma camera and computer system. Posterior, right and left posterior oblique and anterior views were obtained with the patient erect. Regions of interest were defined around each kidney and a background region between and above the kidneys using the posterior and anterior images. Counts within these regions were used to calculate the background-corrected counts from each kidney. The relative renal function (RF) of the right kidney was calculated from the posterior counts using

$$\mathrm{RF}_{(\mathrm{post.})} = \frac{C_{\mathrm{R(post.)}}}{C_{\mathrm{R(post.)}} + C_{\mathrm{L(post.)}}} \times 100\%$$

where $C_{\mathrm{R(post.)}}$ and $C_{\mathrm{L(post.)}}$ are the background-corrected counts from the right and the left kidneys respectively in the posterior view. The calculation was also performed using the geometric mean of the counts from the anterior and the posterior views, so that the relative renal function of the right kidney was given by

$$\mathrm{RF}_{\mathrm{GM}} = \frac{\sqrt{C_{\mathrm{R(post)}} \times C_{\mathrm{R(ant)}}}}{\sqrt{C_{\mathrm{R(post)}} \times C_{\mathrm{R(ant)}}} + \sqrt{C_{\mathrm{L(post)}} \times C_{\mathrm{L(ant)}}}} \times 100\%$$

where $C_{\mathrm{R(ant)}}$ and $C_{\mathrm{L(ant.)}}$ are the background-corrected counts from the right and the left kidneys in the anterior view. The difference between $\mathrm{RF}_{(\mathrm{post.})}$ and $\mathrm{RF}_{\mathrm{GM}}$ was calculated. A difference of less than 5% was considered to be insignificant. The scans were reviewed to see whether there was any obvious anatomical cause to account for any large differences found. For the purpose

TABLE I

Patients studied in each group

| | Group | | | Total |
|---|---|---|---|---|
| | A | B | C | No of patients |
| Age range (years) | 0–12 | 13–20 | > 20 | |
| Females | 68 | 57 | 55 | 180 |
| Males | 29 | 30 | 22 | 81 |
| Total No of patients | 97 | 87 | 77 | 261 |

TABLE II

Difference between the two methods, $RF_{(post)} - RF_{GM}$, for each age group

| | Group | | |
|---|---|---|---|
| | A | B | C |
| Mean difference | −0.74 | −2.14 | −1.37 |
| Standard deviation of difference | 3.4 | 4.29 | 6.64 |
| Variance | 11.59 | 18.46 | 44.2 |

of evaluating the merit of performing the geometric mean calculation in patients of different ages, the patients were divided into three age groups: A (0–12 years), B (13–20 years) and C (more than 20 years).

## Results

A total of 277 DMSA scans have been performed over the past 4 years. The majority of these were carried out for the assessment of renal scarring and divided renal function. Sixteen patients had a solitary kidney and were therefore excluded from this study. Of the remaining 261 patients, 97 were in age Group A, 87 in Group B and 77 in Group C (Table I).

Figure 1 shows the correlation between the relative function of the right kidney as determined from the posterior view only, $RF_{(post)}$, and that calculated using the geometric mean of anterior and posterior views, $RF_{GM}$, for each age group. The correlation coefficients for Groups A, B and C were 0.98, 0.97 and 0.96 respectively. The solid line in each case is the line of identity. The distance of each point from the line of identity represents the difference between the two methods. The mean differences were −0.74%, −2.14% and −1.37% for Groups A, B and C respectively (Table II). Groups B and C exhibited a wider spread (larger variance) than Group A The ratio of the variances (F-ratio test) showed that this increased spread was significant ($p < 0.01$ for Groups A and B, $p < 0.005$ for Groups A and C).

A small group of 10 consecutive scans was analysed independently by three different operators and the spread of these results showed that the analysis technique had a reproducibility of ±0.5% (standard deviation) on relative function. Eight patients in the study had two scans separated by an interval of between 7 months and 45 months. The reproducibility of these repeat investigations was ±2.0% for the posterior view and ±1.6% for the geometric mean method, although part of this variation could be due to genuine clinical change. A change of 5% in relative function would therefore be significant and of clinical relevance.

Table III shows the number of patients with a difference of 5% or more between the two methods of calculation. These comprised eight out of 97 (8%) in Group A, 24 out of 87 (28%) in Group B and 25 out of 77 (32%) in Group C. Review of the DMSA scans demonstrated an obvious cause for this difference in 29 cases (two from Group A, 12 from Group B, and 15 from Group C). The two common causes were malpositioned (*e.g.* low-lying, pelvic or crossed ectopia) and malrotated kidneys. Even when the cases with an

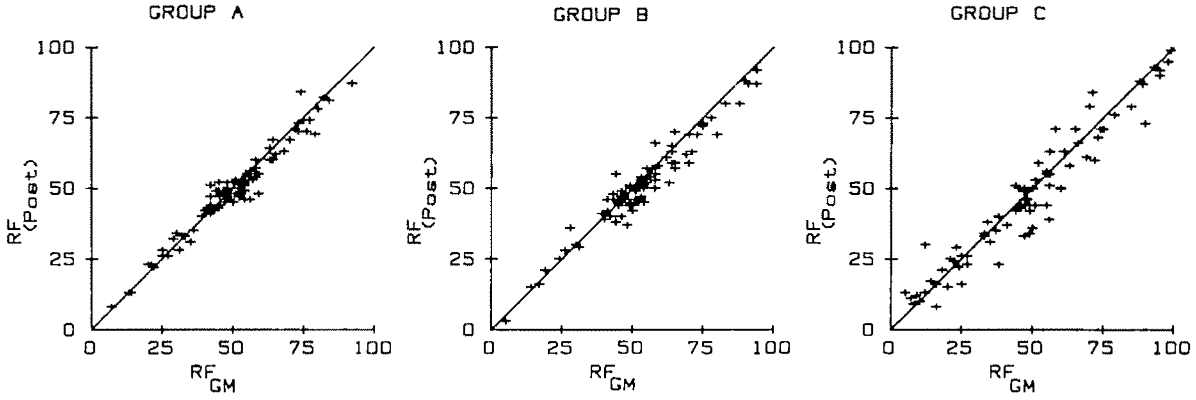

Fig. 1.

Relative function of the right kidney as determined from the posterior view only, $RF_{(post)}$, and by the geometric mean of anterior and posterior views, $RF_{GM}$, for each age group. A (0–12 years), B (0–12 years), B (13–20 years) and C more than 20 years).

TABLE III

NUMBER OF PATIENTS IN EACH AGE GROUP WITH A DIFFERENCE OF 5% OR MORE BETWEEN $RF_{(post)}$ AND $RF_{GM}$

| | Group | | | Total No of patients |
|---|---|---|---|---|
| | A | B | C | |
| < 5% difference | 89 | 63 | 52 | 204 |
| ⩾ 5% difference (with cause) | 2 | 12 | 15 | 29 |
| ⩾ 5% difference (no obvious cause) | 6 | 12 | 10 | 28 |
| Total No. of patients | 97 | 87 | 77 | 261 |

obvious cause are separated from the rest of the group, the proportion of results showing more than 5% difference is still higher in Group B (14%) and in Group C (13%) than in Group A (6%). This result is significant by the $\chi^2$ test ($p < 0.001$).

## DISCUSSION

A number of factors can affect the total DMSA uptake (Taylor et al, 1980), but the differential uptake by the two kidneys should remain the same provided that there is no evidence of ureteric obstruction. If both kidneys lie at the same depth, the observed count rate will be proportional to the DMSA uptake. Differences in renal depth, configuration and rotation will give erroneous results because of the effect of tissue attenuation A 13 mm difference in depth between the two kidneys can produce an error of up to 5% in relative function. An approximate correction for this effect can easily be made by taking the geometric mean of the counts from the anterior and the posterior views. Several workers have commented that the calculation of the geometric mean is more tedious and time consuming than the ratio of the background-corrected counts from the posterior view alone. Born et al (1978) reported that the geometric mean correction of the DMSA data in 39 patients had no effect on the correlation with split creatinine clearance. Powers et al (1981) suggested that from the results of an experimental animal study, the geometric mean correction was probably unnecessary.

Our results show a clinically significant difference between the two methods of calculation in 57 out of the 261 cases (22%). An obvious anatomical abnormality indicating that the geometric mean correction should be applied could be identified in approximately half of these cases. No such abnormality could be identified on the images in 28 cases. Thus, although there are differences in renal configuration and rotation which can immediately be identified, there are also more subtle differences in renal depth which are not readily visible

The geometric mean correction could give an erroneous result if the total attenuating path length through the patient was different at the two kidney sites. However, a 5% error would require, for example, a 27 mm thickness of bowel gas overlying one entire kidney with none over the other, and this is thought to be unlikely. Another possible cause of error could arise from activity in organs, such as the liver, overlying one kidney. This would affect the anterior view more than the posterior but calculations show that liver activity would have to reach 20% of kidney activity in order to produce a 5% difference between the posterior and geometric mean results. No liver activity approaching this level has been seen on any of the scans.

It is interesting to note that, even allowing for the fact that there were more malpositioned and malrotated kidneys in the older age groups (B and C), the number of cases with more than a 5% difference between the two methods of calculation was still significantly higher in these two groups. It is not surprising that the geometric mean correction is less important in children than in adults, since children have a smaller renal depth and any differences will be less important. This could account for the lack of benefit from the geometric mean correction on data obtained from animal studies observed by some workers.

To avoid inaccurate results, we would suggest that the geometric mean correction be applied in all cases when calculating differential renal function using DMSA If the geometric mean correction is applied only when there is evidence of a malpositioned or malrotated kidney, our results suggest that erroneous results will still be obtained in 6% of children under 13 years and in 13% of the older patients.

The same problem will occur when measuring relative renal function using either $^{123}$I-hippuran or $^{99}Tc^{m}$-DTPA. However, since these agents require dynamic studies, it is not so easy to obtain both posterior and anterior views. Usually the extra effort involved in correcting for kidney depth in these studies is not justified unless an anatomical abnormality is seen. However, with static DMSA scanning the anterior image is usually acquired anyway and the geometric mean correction requires very little additional effort.

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# Book reviews

*Nuclear Medicine in Clinical Oncology Current Status and Future Aspects.* Ed. by Cuno Winkler, pp. xvii+420, 1986 (Springer-Verlag, Berlin), DM198.
ISBN 3-540-16164-3 (Berlin)
0-387-16164-3 (New York)

This book contains the papers presented at a symposium, held in May 1985, covering all aspects of nuclear medicine applied to clinical oncology. The contributors were mainly from well known European centres, but some leading American experts were also present Some of the papers are invited reviews and others present original research.

Introductory papers on the technical principles of tumour imaging, including nuclear magnetic resonance, are followed by extensive coverage of the clinical application of these techniques Conventional gamma-camera imaging of different organ systems is reviewed in the light of currently available alternatives; there are a number of papers on newer radiopharmaceuticals, including metaiodobenzylguanidine, and an extensive section on immunoscintigraphy using radiolabelled antibodies. There are short sections on the application of nuclear magnetic resonance and positron emission tomography for tumour imaging. A series of papers on tumour markers measured *in vitro* is more obviously related to clinical oncology than to nuclear medicine An extensive section on therapeutic uses of radiopharmaceuticals covers both well established applications such as $^{131}$I in thyroid carcinoma and more experimental approaches including metaiodobenzylguanidine, strontium 89 and radiolabelled antibodies.

The quality of production of the symposium proceedings is excellent The papers read well, contain good illustrations and are in general well referenced This will be a useful reference work in the library of any department with a significant commitment to imaging oncological patients or research in this field.

E. P. WRAIGHT

*Bone Scanning in Clinical Practice.* Ed by Ignac Fogelman, pp. xviii+260, 1987 (Springer-Verlag, London), £115.00.
ISBN 3-540-16212-7 (Berlin)
0-387-16212-7 (New York)

This volume provides an up-to-date and comprehensive review of the clinical role of bone scanning. As the editor states, the $^{99}$Tc$^{m}$-labelled diphosphonate bone scan remains the most frequently requested investigation in the vast majority of nuclear medicine departments. This stems from its unique sensitivity and the ease with which whole-body skeletal surveys can be undertaken.

The book is organised into 17 chapters followed by a good subject index. It draws on the experience of well known contributors from both sides of the Atlantic, and it comprehensively covers the main aspects of the clinical utility of the radionuclide bone scan. Primary bone tumours, scanning in metastatic disease, metabolic bone disease, Paget's disease, infection, trauma, arthritis, avascular necrosis, orthopaedics and paediatrics are all subjects which are extensively discussed, well referenced and beautifully illustrated. There are interesting contributions discussing the soft-tissue uptake of bone agents, the quantitative aspects of bone scanning, and the measurement of bone mineral by photon absorptiometry

The book is addressed to clinicians and their needs and interests, and it fulfils the role admirably. The volume will be of value to nuclear medicine specialists, radiologists and specialist physicians in endocrinology, rheumatology, orthopaedics and oncology

Springer-Verlag is known for its superb productions but also for its high costs, and this volume at £115 00 does not escape the rule Libraries should be encouraged to purchase this book for future reference, particularly since it is not likely to be overtaken by progress in the immediately foreseeable future

P. J ELL

1987, *The British Journal of Radiology*, 60, 873–875 SEPTEMBER 1987

# Detection of splenosis by radionuclide scanning

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(*Received June 1986 and in revised form December 1986*)

ABSTRACT

Splenosis is the autotransplantation of splenic tissue following trauma. The presence of residual nodules following splenectomy has been investigated by a sensitive scanning method employing reinjection of $^{99}$Tc$^{m}$-labelled, heat-damaged autologous erythrocytes Splenosis was detected in 11 of 19 patients who had had splenectomy for traumatic rupture of spleen. Four of them had multiple nodules, the others a single nodule In one case, the splenic nodule did not take up the sulphur colloid, although it could be visualised on selective splenic scan. We found no splenic nodules in 23 patients who had splenectomy for non-traumatic reasons. It is concluded that the key factor in splenosis is trauma.

Autotransplantation of splenic tissue following trauma is termed splenosis. Implants of ruptured splenic pulp are frequently located in the peritoneal cavity, omentum, mesentery and serosal surface of the intestine or, less frequently, if a route of escape is provided, extraperitoneally. Splenosis is often encountered as a random finding at autopsy or abdominal operation many years after splenectomy.

Splenosis does not have a characteristic clinical picture and in the past a suitable diagnostic method was not available. Since the implants are similar to spleen both in structure and in function, visualisation by radionuclide scanning is useful in the diagnosis (Mackie & Miller, 1973; Spencer et al, 1981; Vega et al, 1981; Dijkstra & Langevcort, 1982).

In this study, we have investigated the presence of splenic nodules in splenectomised patients by a sensitive scanning method employing reinjection of $^{99}$Tc$^{m}$-labelled, heat-damaged autologous erythrocytes.

## MATERIALS AND METHODS

The series consisted of 19 cases (all male), who had had splenectomy for traumatic rupture of the spleen. Their ages ranged from 16 to 40 years. The reasons for splenectomy were. car accident, 11; stabbing, four; gun shot, two; and crush injury, two. A second group of 12 men and 11 women who had splenectomy for non-traumatic reasons (15 for thalassaemia, two for congenital spherocytic anaemia, two for autoimmune haemolytic anaemia and four for other causes of hypersplenism) was also examined. Their ages ranged from 8 to 30 years.

The labelling method used was that described by Armas et al (1980). Thirty minutes after intravenous injection of sterile stannous chloride (0.5 mg), 6 ml of venous blood was taken from each patient into a sterile tube containing 50 units of heparin. Two millicuries (74 MBq) of Na $^{99}$Tc$^{m}$ pertechnetate was added and incubated at 37°C for 15 min, then at 49–50°C for 35 min and then reinjected into the patient. Approximately 2.5 h later, the abdomen was imaged using a gamma camera with a diverging collimator. Anterior, lateral and posterior views were taken in each case, 300 000 counts being recorded.

## RESULTS

Splenosis was detected in 11 of 19 patients (58%), who had had splenectomy for traumatic rupture of spleen. In four of them (21%), the number of splenic nodules ranged between two and 10. Only one nodule was found in each of the remaining seven patients (37%).

Figures 1 and 2 illustrate some cases following splenectomy for trauma. Nodules were found most frequently in the left upper quadrant, especially in patients with a single nodule. However, one patient had a single nodule adjacent to the inferior surface of the right lobe of the liver (Fig. 2). Technetium-99m sulphur colloid scanning, which was performed to locate accurately the splenic tissue in relation to the liver, was normal in this patient, presumably because of the nodule's inability to trap sulphur colloid. Of the 19 patients who had splenectomy for traumatic reasons, in the 11 with splenosis the mean time interval between splenectomy and scanning was 34.2 months (14–96 months) and 19.9 months (3–37 months) for the subgroup in which no signs of splenosis were found.

No nodules were found in the 23 patients who had splenectomy for non-traumatic reasons. In this group the mean time interval between splenectomy and scanning was 52.1 months (19–108 months).

## DISCUSSION

Splenosis is an unusual complication of splenic injury. It rarely has clinical significance. It has been randomly encountered at operation and autopsy and

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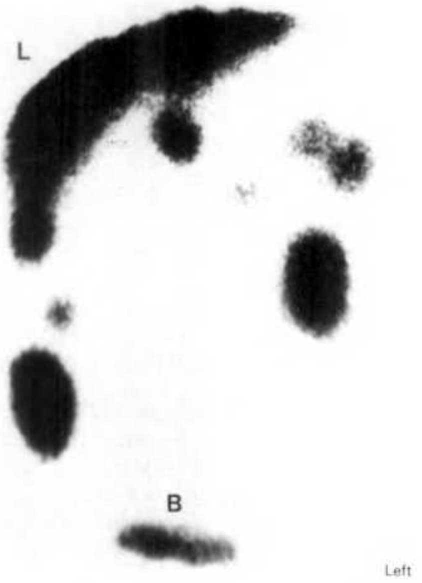

FIG. 1.

Multiple splenic nodules can be visualised in the selective splenic scan done by using $^{99}$Tc$^{m}$-labelled red blood cells (L = liver; B = bladder).

has been reported in a few articles (Jacobson & De Nardo, 1971; Widmann & Laubscher, 1971; Brewster, 1973; Fleming et al, 1976; Boehm & Wybitul, 1980). Since direct examination of the peritoneal cavity was the only method of detecting the condition before splenic scanning was introduced, it had been regarded as uncommon. Up to 1973, a total of 75 cases of splenosis had been reported in the literature (Brewster, 1973).

Pearson et al (1978) reported evidence of renewed splenic activity in 59% (13 out of 22) of splenectomised patients, the majority of whom were children. In five of these, this observation was confirmed by a $^{99}$Tc$^{m}$ sulphur colloid spleen scan. Spencer et al (1981) found that 44% (eight out of 18) of patients in the post-trauma group had splenosis. Nielsen et al (1981) found a similar ratio. In our study, we found that the incidence of positive splenic scan after post-traumatic splenectomy was 58% (11 out of 19). Although our results are similar to Pearson's, we used heat-damaged, $^{99}$Tc$^{m}$-labelled red blood cells, a method similar to Spencer's. In one of our cases, when the $^{99}$Tc$^{m}$ sulphur-colloid technique was used to evaluate the position of a splenic nodule in relation to the liver, we demonstrated that it did not take up the sulphur colloid, although it could be visualised on selective splenic scans (Fig. 2).

In the first group, the time interval for those with a positive scan (34.2 months) was found to be longer than in those with a negative scan (19.9 months). Although this may suggest that the occurrence is related to the length of time following splenectomy, one of our cases, with a period of only 14 months between splenectomy and the diagnosis of splenosis, demonstrates that this is not always the case. It has also been reported that the period can be as short as 5 months (Zeifer et al, 1960). The cases in which we detected 10 and four splenic nodules had the longest interval since trauma in the group and we suggest that the time interval between rupture and diagnosis of splenosis may affect the number of nodules visualised. The critical point here may be that the splenic nodules reach a size which can be imaged by a scan only after a certain period of time. It is reported that these nodules may range from a few up to 400 in number, and from pinpoint to several centimetres in size, but they must reach a diameter of 2.5 cm before they can be seen on scans.

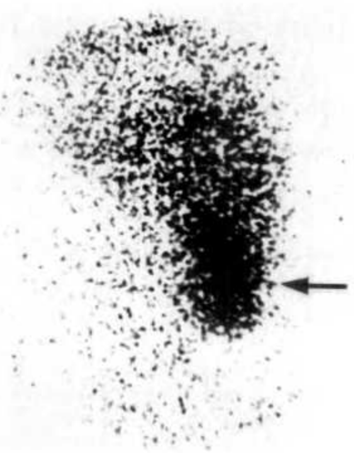

FIG. 2.

Selective splenic scan shows a splenic nodule (arrow) adjacent to the inferior margin of the right lobe of the liver.

The key factor in splenosis is trauma, but splenectomy leads to splenosis since it calls for overfunctioning of implants (Jacobs et al, 1963). The same mechanism also leads to the hypertrophy of an accessory spleen (Spencer et al, 1981). Differential diagnosis between splenosis and accessory spleen is not possible using radionuclide techniques.

In order to determine the incidence of accessory spleen, another group of patients who had had splenectomy for non-traumatic reasons was also included in our study. In this group, none of the patients showed scintigraphic evidence of splenosis. This indicates that trauma itself, and not simply splenectomy, is important in the occurrence of splenic nodules.

In conclusion, we found that 58% of patients in the post-trauma group and 0% of patients in the non-traumatic group had splenosis, and demonstrated that selective splenic scanning provides enough evidence to refute the prevailing opinion about the incidence rate of splenosis.

ACKNOWLEDGMENTS

The authors gratefully acknowledge Ms Aydan Aras for editorial help and Mr Atilla Danlgen for the photography.

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# Book reviews

*Living Anatomy A working atlas using computed tomography, magnetic resonance and angiography images* By R A Novelline and L F. Squire, pp. x+117, 1987 (Hanley & Belfus, Philadelphia, C.V. Mosby Co., St Louis), £23.50.
ISBN 0-932883-03-6

Books with the name Lucy Frank Squire in the authorship are never dull, and usually novel. This one aims to supplement the classic anatomical textbooks by introducing the medical student to a series of computed tomography and magnetic resonance scans (yes, why not introduce them to the newest modality on day one?) The head, face, neck, thorax, abdomen and pelvis are amazingly well covered in 118 large, atlas-sized pages. Upper and lower limbs are not included.

The format is designed as a self-instructional, problem-solving approach Problems and answers are on facing pages, an arrangement I found more convenient than the "answer over the page" method. Occasional angiograms enliven the teaching.

A particular strength of this atlas is the use of the same patient for contiguous slices, where possible, and the placement of accurate (and well matched) line drawings adjacent to the appropriate computed tomography image. The use of red arrowing and occasional red lettering, plus the presence of large bold print throughout, make this an attractive book, which looks uncluttered.

At £23.50, this is a good buy. Although aimed at medical students, radiologists would find it a useful reference manual of normal computed tomography and magnetic resonance anatomy. ROBERT DICK

*Radiology of Diabetes.* By B. E. Eyes and I. A. MacFarlane, pp. vi+76, 1986 (MTP Press Ltd, Lancaster), £13.50.
ISBN 0-85200-936-4

The preface of this small volume states that it is intended to help clinicians in training who are involved in the management of diabetic patients; but if further information is required they are then advised by the authors to consult more comprehensive radiological or clinical texts.

It is hard to imagine when it would be helpful to interpose a consultation with this small book. It is 72 pages in length, of which 50 pages are devoted to simple radiographic or ultrasound images. They are divided into eight system-orientated groups, each preceded by a page or two of introductory text

Quality of the reproduction of the radiographs is on the whole good, but many of the films have little direct relationship to diabetes, *e.g.* calcified gallstones and carcinoma of the colon, and many of the annotations are rather vague, for example bony destruction of the terminal phalanx of the great toe would not be regarded as "early" changes of osteomyelitis in many departments

Your reviewer did not feel qualified to comment on much of the text, despite its brevity, and therefore an opinion was sought from a diabetological colleague. He was unable to agree with a number of the points made and felt that statements such as "a few spoonfuls of sugar should prevent hypoglycaemia" would give many diabetologists (and several of their patients) fits. He also commented on the propensity for grammatical errors and had to disagree with the definition of the diagnosis of diabetes which he felt had completely ignored the WHO criteria.

The book is also characterised by the complete absence of reference to any other publication and it would be difficult to recommend it to potential readers without a guide as to where they should go for more comprehensive information, which the authors themselves had advised as likely in their preface

H W LOOSE

*Multiple Choice Questions in Radiology With answers and explanatory comments.* By P R Patel, pp vii+71, 1986 (Edward Arnold, London), £4.25.
ISBN 0-7131-4501-3

This small paperback contains 205 multiple-choice questions, each arranged in the style of the F.R.C.R. final examination. They differ from the F R.C R. multiple-choice question papers in that Dr Patel has grouped them into seven subspecialty sections and has also provided answers and short notes on the facing pages.

Multiple-choice questions are not easy to set. the stem statement must be concise and clear and addition of any one of the branches must result in a grammatical question which allows a true or false answer based on the mainstream medical knowledge of the day. In general, the multiple-choice questions in this volume meet these criteria but it is unfortunate that "may" is used in the stem of two of the first five questions; ambiguity is invariably produced by the use of this word and it should be avoided in this context Despite this unfortunate opening, the questions given are generally good and will provide an excellent introduction to and practice in multiple-choice questions in radiology. It can be recommended to candidates for the final F.R.C R. examination

MICHAEL RUTTLEY

1987, *The British Journal of Radiology*, *60*, 877–879 SEPTEMBER 1987

# The visible wall of a main bronchus: a new radiological sign of pneumomediastinum

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(*Received July 1986 and in revised form November 1986*)

ABSTRACT

A new sign of pneumomediastinum (mediastinal emphysema), namely a visible wall of a main bronchus as seen in the mediastinum on frontal radiographs of the chest, is described This sign was present in eight out of 20 random cases of pneumomediastinum in adolescents and adults

The radiological diagnosis of pneumomediastinum is usually easy if conventional frontal, penetrated frontal and lateral radiographs are available and various signs have been described to differentiate it from air in the oesophagus (Meredith et al, 1981) and from pneumopericardium (Cyrlak et al, 1984). This paper describes a new sign—the visible wall of a main bronchus. It was present in 40% of the cases we analysed and was more prominent on the left.

## MATERIAL

Our index case was a 15-year-old boy who presented with an attack of asthma. Radiographs of the chest showed streaky lucent areas of air extending from the mediastinum into the neck, outlining and highlighting the aorta, typical of pneumomediastinum. On the postero-anterior radiograph the walls of the left main bronchus were clearly visible, being demarcated on one side by air in the bronchial lumen and on the other side by air in the mediastinum (Fig. 1).

We have subsequently analysed the frontal chest radiographs of 19 consecutive cases of pneumomediastinum in adults and adolescents (15 males and 4 females) from the teaching files of the Tygerberg and Groote Schuur Hospitals.

## RESULTS

In the 20 cases under review a visible wall of a main bronchus was seen in eight cases. In five cases the walls of only the left main bronchus were seen. In three cases the walls of the left and the right main bronchi were seen. In no case were the walls of only the right main bronchus seen. In two cases the visible bronchial wall sign was the most obvious sign of pneumomediastinum; in the other six cases it was additional evidence

## DISCUSSION

In pneumomediastinum, from whatever cause, air may be localised in one or more parts of the mediastinum or spread, to a lesser or greater degree, to surround mediastinal structures. Air may also dissect parietal pleura from mediastinal structures, displace mediastinal structures, or spread outside the mediastinum. In rare cases it may impede systemic and pulmonary venous return to the heart and exert pressure on the heart.

Numerous radiological signs of pneumomediastinum (below) have been described.

(1) Vertical radiolucent streaks may separate and outline the soft-tissue layers and structures of the mediastinum (Sutton, 1980).
(2) A lucent zone varying in width from less than 1 mm to a few centimetres may surround the heart shadow on frontal views (Simon, 1971; Van Stiegman et al, 1977; Sutton, 1980; Maunder et al, 1984).
(3) On lateral views, a sharply defined linear, oval or round area of translucency may be seen between the sternum and the heart, so called "precordial air" or "pneumoprecardium" (Lillard & Allen, 1965; O'Gorman et al, 1968).
(4) Air in the posterior mediastinum may present on frontal views as a well circumscribed, oblong area of increased translucency centred in the mid-sagittal plane (Bowen & Quattromani, 1980) and on lateral views as a sharply defined area of increased translucency behind the heart (Van Stiegman et al, 1977).
(5) Air may outline, surround and sharply delineate the innominate artery, left common carotid artery, left subclavian artery, main pulmonary artery (Lillard & Allen, 1965; Sumerling & Irvine, 1966), left innominate vein, superior vena cava and azygos vein (Sumerling & Irvine, 1966), trachea, large bronchi (Sumerling & Irvine, 1966; Cyrlak et al, 1984), ligamentum arteriosum (Sumerling & Irvine, 1966) and oesophagus (Bowen & Quattromani, 1980).
(6) Air around the aorta may "highlight" the aortic knob (Maunder et al, 1984) and air around the right pulmonary artery may give the "ring around the artery sign" (Hammond, 1984).
(7) The confluence of the innominate veins may be outlined on the frontal views, giving rise to a "V" sign (Cyrlak et al, 1984).
(8) The thymus may be outlined and/or displaced by mediastinal air, giving rise to the "spinnaker sail

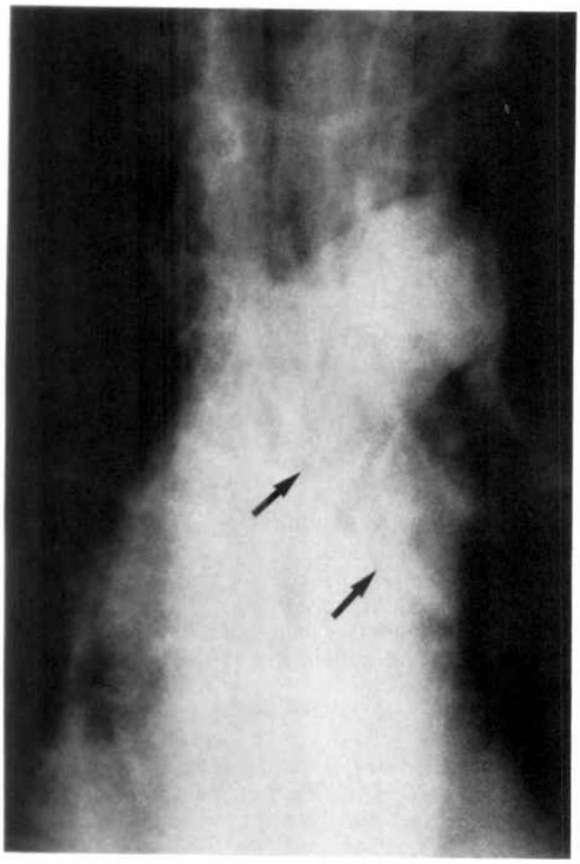

FIG. 1.

Frontal radiograph of mediastinal region showing pneumomediastinum with linear transradiances well seen above the aorta, which is itself outlined by air. The medial wall of the left main stem bronchus is outlined on both sides by air (arrows).

sign" (Moseley, 1960) and the "rocker-bottom thymus" (Kogutt, 1981).

(9) Air may extend between the pericardium and the diaphragm, giving rise to the "continuous diaphragm sign" (Levin, 1973).

(10) Air may extend beyond the confines of the mediastinum. It may elevate the diaphragmatic pleura from the diaphragm, giving rise to a round, oval or slit-like lucent space (Lillard & Allen, 1965; O'Gorman et al, 1968; Sutton, 1980). In the lower posterior mediastinum it may elevate the mediastinal and diaphragmatic pleurae, giving rise to a "V" sign (Naclerio, 1957) or it may be confined mainly to one or both inferior pulmonary ligaments (Volberg et al, 1979).

Because the radiological signs of pneumomediastinum in the neonate differ in appearance and frequency from those in the adolescent and adult (Volberg et al, 1979; Sutton, 1980; Cyrlak et al, 1984) we have confined our investigation to the latter.

To the best of our knowledge, the visible wall of a main bronchus, as described here, has not yet been reported as a sign of pneumomediastinum. This is surprising, as a visible wall of a main bronchus is exactly what one would expect to see when there is air both in the lumen of a main bronchus and surrounding it.

Normally the wall of a main bronchus in the mediastinum is seen as an interface between air in the lumen and the surrounding mediastinal soft tissues and the thickness of the bronchial wall is not outlined. The thickness of the bronchial wall can, however, be seen when it is surrounded by air. The sign described here is similar to and must not be confused with what may at times be seen on frontal chest radiographs when there is air in a segment of the oesophagus. Exceptionally, a segmental air oesophagogram in the infra-aortic region associated with distension of the oesophagus and its displacement to the left may produce visualisation of the lateral wall of the left main bronchus (Cimmino, 1965). When there is associated herniation of the azygo-oesophageal recess of the right lung across the midline, both the lateral and the medial wall of the left main stem bronchus may be visualised (Meredith et al, 1981).

It is sometimes difficult to distinguish between pneumomediastinum, which is usually a benign condition, and pneumopericardium, which is often fatal. It may well be that many cases reported as pneumopericardium were in fact cases of pneumomediastinum (Cochrane, 1983). The "visible main bronchial wall" sign, when present, is expected to differentiate between pneumopericardium and pneumomediastinum because air in pneumopericardium is unlikely to abut on the wall of a main bronchus and therefore should not give a "visible main bronchial wall" sign.

*Editorial comment*

The medial wall of the right main stem bronchus may be outlined by air containing lung or fat (Muller et al, 1985) and it would seem wise to consider the "visible main bronchial wall sign" described by Beyers and Melonas as applying only to the left main stem bronchus. This does not detract from their observation, as in all eight positive cases the left main stem bronchus was involved.

## ACKNOWLEDGMENT

We wish to thank Professor R. E. Kottler, Groote Schuur Hospital, Cape Town, for allowing us access to his teaching files and Professor B. J. Cremin of the Red Cross Hospital for constructive comments.

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# Book reviews

*Atlas of Tumors of the Facial Skeleton Odontogenic and Nonodontogenic Tumors.* By J. Prein, W. Remagen, B. Spiessl and E Uehlinger, pp. x+162, 1986 (Springer-Verlag, Berlin), DM368
ISBN 3-540-16167-8 (New York)
0-387-16167-8 (Berlin)

Most tumours of the facial skeleton are sufficiently uncommon for an accurate appraisal of their epidemiology and clinical behaviour to be problematical. The development of oral radiology as a specialty within dental schools has helped to clarify the diagnostic criteria but the fact that radiographs of such cases are frequently reported as "radiographs enclosed" is a reflection of the absence of comparable expertise outside such specialist centres For this reason the publication of this atlas by DOSAK, the German-Austrian-Swiss Association for the Study of Tumours of the Face and Jaws, is to be welcomed.

It is based on 1256 cases collected since 1971 and consists of a text generously illustrated by representative radiographs and histopathology, a format that is highly praiseworthy since, to their own regret, pathologists are often forced to assess in isolation biopsy specimens of what may be untypical areas of a lesion But despite the high standard of reproduction (the radiographs more so than the histopathology) the value of this book for the questing radiologist is limited The title notwithstanding, the book covers both neoplasms and the non-neoplastic tumour-like lesions of the jaws, the latter term covers both the odontogenic lesions such as the dens in dente, an anomaly of dental development, and dental cysts and under "non-odontogenic" conditions, such as fibrous dysplasia and the solitary and aneurysmal bone cysts The relative numbers of lesions recorded do not in fact bear much relationship to their clinical prevalence, suggesting some vagaries in reporting, dens in dente, for instance, is the most common of the odontomes but only one case is recorded here, while radicular cysts have been shown to be more common than follicular cysts and odontogenic keratocysts (it is not clear why these two have been grouped together) The chapters on odontogenic tumours follow what is termed the sequence of histopathological relationships, those on non-odontogenic the German Bone Tumour Key; neither will be of much help to the radiologist whose diagnostic thought processes run on entirely different lines

The radiographic descriptions are limited to certain features, whether radiolucent or radiodense, uni- or multilocular and the presence or absence of root resorption Other useful diagnostic features (displacement of teeth or the inferior dental canal, expansion rather than erosion of the lateral antral wall) are not mentioned and this also detracts from the usefulness of this atlas. Further, the attitude repeatedly expressed towards differential radiographic diagnosis is unduly pessimistic· not all lesions in the jaws look the same and there are specific features that will help the radiologist to arrive at, if not the correct diagnosis, then certainly the correct ball-park In summary, a worthy book but offering little that is relevant to the needs of a general, or even a head and neck, radiologist.

P. N HIRSCHMANN

*Computed Tomography of the Cranial Skeleton (Face and Skull). Exercises in radiological diagnosis.* By Marcelle Mégret, pp viii+168, 1986 (Springer-Verlag, Berlin), DM35
ISBN 3-540-15389-6 (Berlin)
0-387-15389-6 (New York)

*Computed Tomography of the Craniofacial Skeleton (Face and Skull)* by Marcelle Mégret is a series of exercises in radiological diagnosis of conditions causing bony changes involving the skull vault and base and the orbit and sinuses. The book is arranged in two main sections The first half covers normal anatomy, followed by examples of different pathology using axial computed tomography (CT) scans, mainly windowed for bone structure. There are also a few coronal (direct and reformatted) and sagittal reformats. The second half consists of a descriptive section with line drawings corresponding to the examples in the first section In a book of this size, in which half is taken up with normal anatomy, the pathological section appears fragmented Although it is aimed at those with a fairly low level of knowledge, in many of the cases the diagnosis is not specific and some examples are by no means typical of the conditions they demonstrate.

The bone images are all in the reversed mode to that normally used in the English speaking world and have been undertaken on a CT scanner which produces poor images by today's standards The text is particularly verbose and it is apparent that the author's mother tongue is not English as the text contains words which are not used in English The general layout is cumbersome and difficult to use as an examination text and it is surprising that the publishers have not demanded a higher quality of imaging. It is unlikely that students will be motivated to read this book once, let alone using it as a refresher course which is its apparent intention. I cannot see that it really has a purpose and so I cannot recommend its purchase

DEREK KINGSLEY

*Pocket Atlas of Normal Ultrasound Anatomy* By Matthew D Rifkin and Larry Waldroup, pp. 70, 1985 (Raven Press, New York), $14 50
ISBN 0-88167-163-0

This very small pocket atlas contains 53 figures, almost all of which are produced with a manually operated static scanner Many are compounded· the transverse scans of the abdomen are very heavily compounded and can hardly be said to be state of the art. Images presented in the book include those of the neck, abdomen and pelvis There is no text

It is difficult to see any value in such a book and I have to confess to not entirely agreeing with the authors in their labelling of many of the structures The gluteus maximus is apparently seen on four different anterior scans of the pelvis Can this really be so?

The book is said to be "an invaluable guide to interpreting ultrasound images" I doubt it

HYLTON B MEIRE

1987, *The British Journal of Radiology*, 60, 881–886 SEPTEMBER 1987

# A method for thresholding subtracted images in radiolabelled-antibody imaging

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*(Received November 1986 and in revised form January 1987)*

ABSTRACT

The low target-to-background ratio of radiolabelled antibodies often necessitates the use of a subtraction technique to enhance areas of tumour uptake However, interpretation of the results is often difficult due to noise in the antibody and subtraction images. By performing a linear, least-squares fit to all the pixel values, it is possible to calculate the "prediction interval" This may be used as a variable threshold for the subtracted image to leave only statistically significant counts. The method has been evaluated in models and found to be independent of count density and image processing. Useful results have been obtained in initial patient studies. The technique is fast and objective, and therefore it may have a useful role in the routine analysis of subtracted images

Considerable interest has been shown in the localisation of tumours using radiolabelled antibodies. Tumours of the gastrointestinal tract (Goldenberg et al, 1978), thyroid (Fairweather et al, 1983a), germ-cell tissue (Halsall et al, 1981; Goldenberg et al, 1981) and insulinomas (Fairweather et al, 1982) have all been localised using $^{131}$I-labelled antibodies Alternative radiolabels such as $^{111}$In (Fairweather et al, 1983b) and $^{123}$I (Epenetos et al, 1982) have been proposed However, despite its physical disadvantages, $^{131}$I remains widely used since the labelling procedure is simple, the half-life convenient and, provided suitable blocking agents are administered, there is no specific organ uptake.

In practice, a large proportion of the administered dose remains in circulation and in other normal tissues, and this may obscure specific tumour uptake. Subtraction techniques have been proposed (Goldenberg et al, 1980; Deland et al, 1980) using a combination of $^{99}$Tc$^{m}$-human serum albumin and pertechnetate to simulate the non-specific distribution of labelled antibody. After normalising for the differences in counts in the two images, the $^{99}$Tc$^{m}$ image is subtracted from the $^{131}$I image to enhance any areas of specific uptake.

The subtraction procedure may result in ambiguous results (Ott et al, 1983) notably due to poor imaging statistics. Various methods have been proposed to improve the display of the subtracted images. These have included statistical analysis of selected suspicious regions (Green et al, 1984), dynamic variable background subtraction (Wahl et al, 1986), spatial probability mapping (Nimmon et al, 1984) and maximum entropy deconvolution (Fairweather et al, 1983c).

These methods have not found routine use due to either lack of objectivity or lengthy analysis times. As well as being fast and objective, a method of analysis needs to take account of different count densities (as these will result in different noise levels throughout the image) and any image processing techniques (for example, the number of smooths) which have been applied to the images.

We have developed a method for calculating a threshold for the subtracted image which varies with count density. This is derived from a statistical analysis of the individual pixel values in each pair of $^{131}$I and $^{99}$Tc$^{m}$ images.

## MATERIALS AND METHODS

### *Patients and imaging*

Patients received intravenously 37–74 MBq (1–2 mCi) $^{131}$I-labelled antibodies. Images were obtained 24 h and 48 h post-injection. Prior to each imaging study, the patient also received 37 MBq (1 mCi) each of $^{99}$Tc$^{m}$-pertechnetate and human serum albumin 30 min and 5 min respectively before imaging. To block uptake of free iodine in the thyroid, patients were given oral doses of potassium iodide (60 mg 8-hourly) commencing 24 h before administration of the labelled antibody and continuing for a week. Potassium perchlorate (200 mg 6-hourly) was also given, commencing 24 h before the first scan and continuing until after the second scan, to block non-specific uptake of $^{99}$Tc$^{m}$ by the stomach and salivary glands (Bradwell et al, 1983)

Anterior and posterior images of chest and abdomen were acquired using a CGR Gammatome gamma camera fitted with a high-energy (400 keV) collimator and linked to a DEC PDP 11-34 computer. Five-minute images are obtained simultaneously of the $^{131}$I and $^{99}$Tc$^{m}$ distributions using 20% windows centred on 364 keV and 140 keV photopeaks respectively. Images are stored on the computer as a 64 × 64 matrix.

### *Subtraction technique*

The value of each pixel in the $^{131}$I image is compared with the count in the corresponding pixel in the $^{99}$Tc$^{m}$

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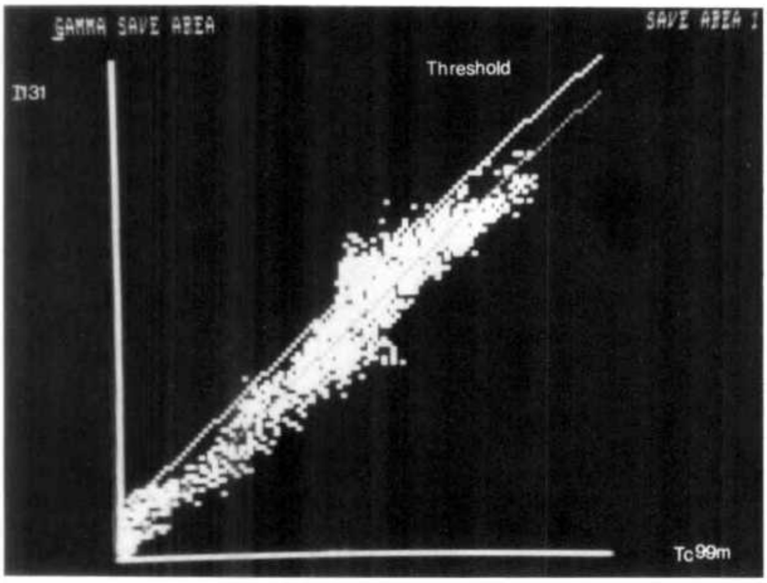

FIG. 1.
Relationship between $^{131}$I and $^{99}$Tc$^{m}$ pixel counts showing fitted line and threshold.

image. Any pixel in either image containing zero counts is ignored to avoid contributions from background.

The equation:

$$I_n = kT_n + c$$

may then be fitted to the data using a linear least-squares technique, where

$I_n$ is the $n$th pixel value in the $^{131}$I image
$T_n$ is the corresponding pixel value in the $^{99}$Tc$^{m}$ image
$k$ is the slope and
$c$ is the intercept

The value $k$ represents the normalising factor between the two images. In practice, the intercept is close to the origin but is not necessarily zero.

The analysis also allows the calculation of the prediction interval (see Appendix) shown in Fig. 1, at a probability level of 95%. For a particular $^{99}$Tc$^{m}$ pixel count, this represents the range in which the corresponding $^{131}$I pixel count should lie if there were no specific tumour uptake. Any $^{131}$I pixel counts lying above this range will therefore be due to tumour uptake. A small contribution from noise will remain, but only with a very low probability. It is assumed that the number of tumour pixels is small compared with the number of pixels in the rest of the image.

The upper limit of the prediction interval may therefore be applied as a variable threshold to the $^{131}$I image to leave only statistically significant counts. In practice, two images are produced: a subtracted image where each pixel value ($S_n$) is given by

$$S_n = I_n - kT_n$$

and a thresholded image where each pixel value ($H_n$) is given by

$$H_n = I_n - \mathrm{PE}\,(T_n)$$

where PE ($T_n$) is the 95% prediction interval for the value $T_n$.

## PHYSICAL EVALUATION

### *Effect of count density*

To test the effectiveness of the prediction interval at removing non-significant counts, images were obtained of a lead bar phantom using a $^{57}$Co source. The bar phantom was chosen as a suitable test object as it contained a range of pixel counts similar to that obtained from an antibody image. An image containing 600 000 counts was used to simulate a typical $^{99}$Tc$^{m}$ image (subtraction image), and images ranging from 100 000 to 300 000 counts to simulate the typical count densities of $^{131}$I-antibody images (target image).

Subtracted and thresholded images were produced from the target and subtraction images as described above. The number of non-zero pixels remaining after thresholding were expressed as a proportion of the number of non-zero pixels in the original image.

### *Effect of smoothing*

Subtraction images containing 600 000 counts and target images containing 200 000 counts were used. Each image was smoothed 0 to 3 times before subtraction, and the proportion of non-zero pixels calculated as before.

### *Effect of tumour size*

It is assumed in the calculation of the prediction interval that the number of pixels covering the tumour

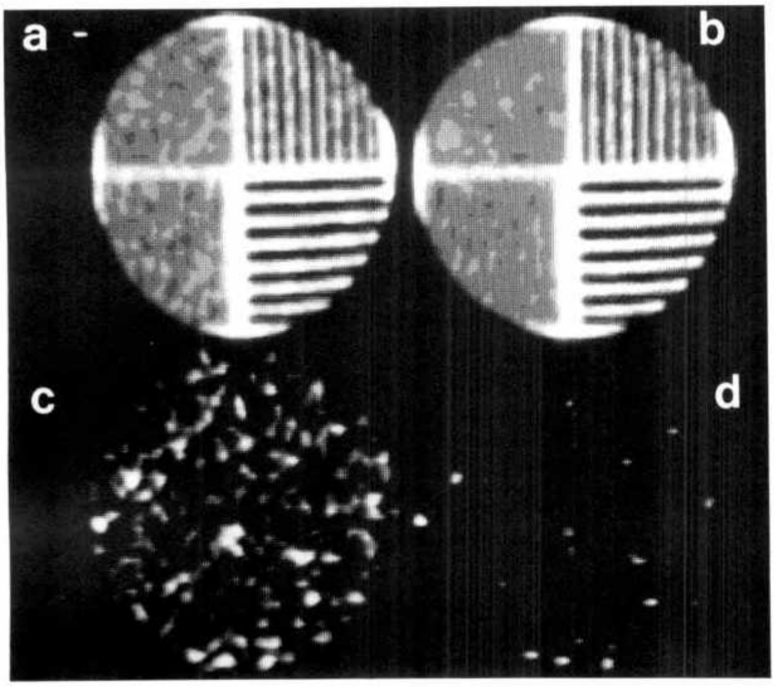

FIG. 2.
Bar-phantom study: (A) simulated $^{131}$I image, (B) simulated $^{99}$Tc$^{m}$ image, (C) subtracted, (D) thresholded.

area is small compared with the rest of the image, and therefore will not affect the threshold. To test this assumption, target and subtraction images of a uniform $^{57}$Co source containing 200 000 and 600 000 counts respectively were used.

Each image was smoothed once, and then a varying number of pixels in the target image had extra counts added to them to represent a tumour. The simulated tumour-to-background ratio was fixed at 1.2, this representing the maximum ratio we have observed on antibody images. In practice, this ratio is often less, and so any effect on the threshold will be less significant than shown here.

The threshold for the mean count in the target image was calculated and expressed as a percentage of the actual tumour count. The variation in threshold with increasing numbers of pixels, representing tumour diameters up to 10 cm, was calculated.

## RESULTS

The correlation between $^{131}$I pixel counts and $^{99}$Tc$^{m}$ pixel counts in a representative image are shown in Fig. 1 together with the fitted straight line and upper limit of the 95% prediction interval. Typically, the correlation coefficient is greater than 0.95 for images which have been smoothed once. Note that the fitted straight line intercepts the $y$-axis just above the origin, most probably due to differences in overall background between the two images. Figure 2 shows the bar phantom images containing 600 000 and 200 000 counts simulating typical $^{99}$Tc$^{m}$ and $^{131}$I images. After subtraction (Fig. 2C), a number of residual counts are left which would be difficult to interpret if this were a clinical study. After thresholding, however, only a very small proportion of counts remain. These pixels appear randomly distributed and do not correspond to low- or high-count areas, demonstrating the variation of the threshold with count density.

Figure 3 shows the effect of varying count densities in the antibody image on the threshold. A mean of 2.8% of pixels are left after thresholding, which is consistent with that expected when a 95% prediction interval is used. Approximately 5% of counts should lie outside the intervals, half above and half below. The effect of smoothing, as shown in Fig. 4, shows slight variations in the threshold, although the proportion of pixels remaining is still between 2.2% and 2.9%.

Figure 5 shows that there is a slight increase in the calculated threshold as the tumour size increases. The threshold increases slowly from 93.5% of the tumour counts to 94.5% up to a tumour size of 6 cm and then slightly faster up to 96.2% at a tumour size of 10 cm.

Figure 6 shows the technique applied to a representative $^{131}$I-anti-CEA image of a patient with a colorectal tumour. Figure 6C, the subtracted image with no thresholding, shows a large tumour area plus a number of residual counts. Application of the threshold (Fig. 6D) removes the non-significant counts while leaving the tumour. No other tumour areas were found at laparotomy.

## DISCUSSION

The fundamental basis behind a subtraction technique is that the subtracting radionuclide distribution is

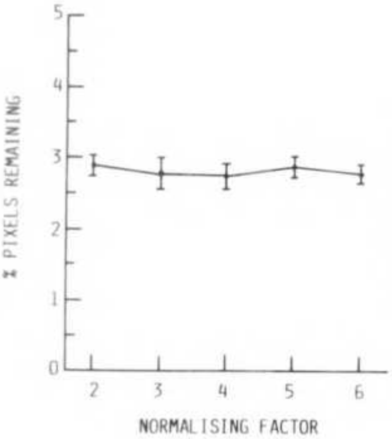

FIG. 3.
Effect of count density on threshold.

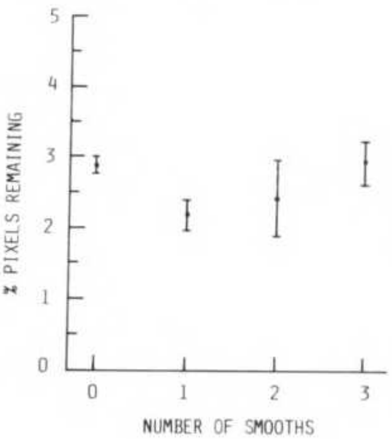

FIG. 4.
Effect of smoothing on threshold.

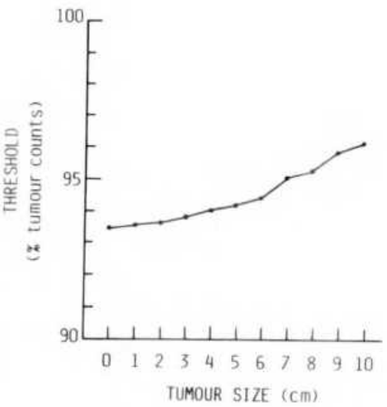

FIG. 5.
Effect of tumour size on threshold.

representative of the target radionuclide distribution. The essentially linear relationship shown in Fig. 1 between the $^{131}$I pixel counts and corresponding $^{99}$Tc$^{m}$ pixel counts supports this assumption, although it is quite likely that small local variations will be masked by the image noise. Differences in gamma energy of the two radionuclides and variations in biological distribution may give rise to artefacts on subtraction (Ott et al, 1983). Local area subtraction (DeLand et al, 1982) may overcome some of these problems, but poor imaging statistics remain a major problem. There remains a clear need for a simple, objective method to establish whether residual counts remaining after subtraction are statistically significant.

Thresholding the subtracted image by calculating the prediction interval appears to be such a technique. It is fast, taking less than 20 s on our system to produce both subtracted and thresholded images, and requires the minimum of operator intervention. It has been shown to be independent of count densities over the

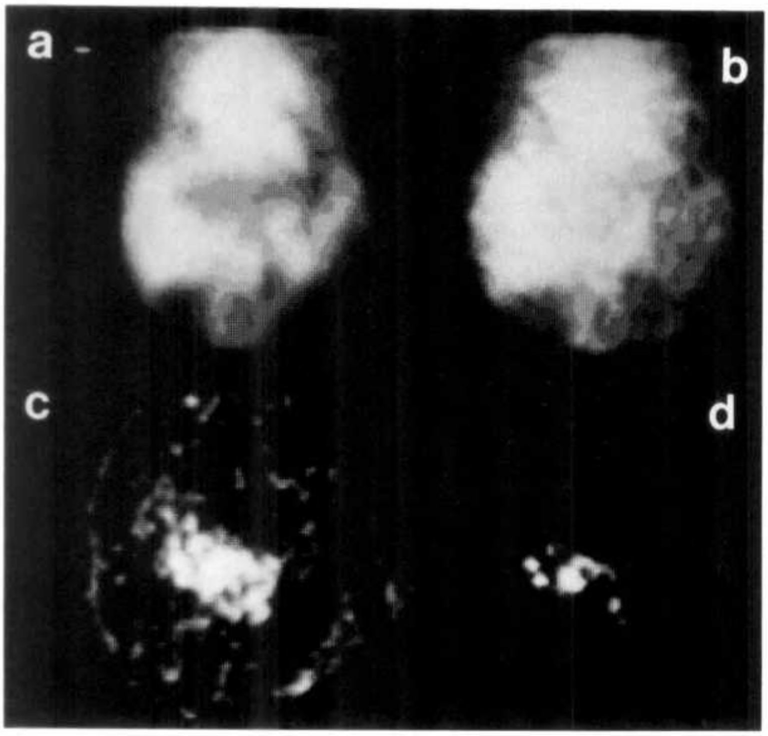

FIG. 6.
$^{131}$I-antibody study: (A) $^{131}$I image, (B) $^{99}$Tc$^{m}$ image, (C) subtracted, (D) thresholded.

range typically obtained in our $^{131}$I-antibody scans. Smoothing the images did show a very slight effect on the calculated noise, possibly due to edge effects or blurring of fine detail

This method is, however, dependent on a number of assumptions. The calculation of the prediction interval assumes that the data are normally distributed and that the variance of $y$-values is constant for all values of $x$. Although noise in an image is represented by a Poisson distribution, there is no simple statistical test for the comparison of Poisson variables. However, the noise does tend to a symmetrical normal distribution at pixel counts typically obtained in antibody imaging. The variance in $y$-values is obviously not constant, but our initial studies using a weighted, least-squares technique appeared to offer little advantage at the expense of longer computing time. Venot et al (1986) have recently described a more sophisticated technique for registration and comparison of two images assuming a Poisson distribution but, again, this requires substantial computing times.

The assumption that the number of pixels containing tumour counts is small compared with the total number of pixels was shown to be true with small tumours. There was a gradually increasing effect on threshold level which became more significant around tumours of 10 cm diameter. However, it is unlikely that a tumour of such a size would present a diagnostic problem on a conventional subtracted image. Furthermore, the effect was calculated using the highest expected tumour-to-background ratio. In practice, this ratio is usually smaller and the effect on the calculated threshold will be correspondingly less.

There are two situations in which a disproportionate difference in counts between areas on the $^{99}$Tc$^{m}$ and $^{131}$I images may exist. Some of the injected activity may be extravasated or rapid excretion of $^{99}$Tc$^{m}$ following injection may give rise to differences in bladder activity. Extravasated activity is not common and may easily be removed from the field of view or shielded. Bladder activity is often removed if the patient voids immediately before imaging commences. However, should this not be successful it is easy to mask out the bladder on the computer images prior to subtraction. The program incorporates a check that the correlation coefficient is greater than 0.95 to prevent an erroneous calculation.

The thresholding technique is now in routine use on antibody scans. The choice of a 95% prediction interval was based on theoretical considerations alone. However, the method can easily be adapted to whatever prediction interval is required by the user, thereby optimising sensitivity or specificity as needed in a specific clinical situation. Further studies are in progress to optimise the thresholding technique for our particular applications.

The technique may also help in modelling certain aspects of the imaging technique by showing, for example, what improvements in tumour uptake or image processing are required to increase significantly the signal-to-noise ratio. A number of other radionuclide imaging techniques may involve subtraction including $^{111}$In-leucocyte imaging (O'Doherty et al, 1985) and parathyroid imaging (Young et al, 1983). Quality control of gamma-camera images also involves the assessment of any significant changes between sequential images. It is possible that this technique may have application in other such areas where image is a problem, providing that the target area is small compared with the total image area.

ACKNOWLEDGMENTS

We would like to thank Mrs M Rooke for her assistance with the typing and the Department of Medical Illustration for the diagrams.

## APPENDIX

*Calculation of prediction interval* (Chatfield, 1978)

For a fitted straight line $Y = kX + c$ there is a probability $1-\alpha$ that a future observation on $Y$ at the point $X_0$ will lie in the range

$$kX_0 + c \pm t_{\frac{1}{2}\alpha, n-2} S_{y/x} \sqrt{1 + \frac{1}{n} + \frac{(X_0 - \bar{X})^2}{\sum_i (X_i - \bar{X})^2}}$$

where $n$ = number of observations, $t_{\frac{1}{2}\alpha, n-2}$ = the appropriate $t$-distribution value (for a probability of 0.95, $t_{\frac{1}{2}\alpha, n-2} = 1.96$ if $n$ is large) and

$$S^2_{y/x} = \sum_i \frac{(Y_i - kX_i)^2}{n-2}.$$

The upper limit of this range PE($X_0$), *i e* the limit of the 95% prediction interval for a value $X_0$, is used as the threshold. In practice, $c$ is small and does not contribute significantly to the calculated threshold.

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# Computer aids to mammographic diagnosis

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(*Received April 1985 and in final form October 1986*)

## ABSTRACT

The improvement of mammographic specificity was investigated by means of identifying specific radiological features Data are presented on the first 500 patients studied who had previously undergone mammography followed by biopsy The presence of specific mammographic features on each radiograph, first determined by retrospective examination, was entered into a computer database Subsequent discriminant function analysis demonstrated the importance of a small number of features whose presence could be used in an algorithm to predict diagnostic outcome Using this algorithm, this feature-identification approach correctly identified 87.6% of benign and 79% of malignant cases. Specificity was improved to 88% as compared with the original radiological diagnosis of 49% It is argued that this approach is very promising and a computer-assisted diagnosis based on these findings is described.

In a mammographic service, continuous attempts must be made to minimise the number of patients who are referred for biopsy or follow-up examinations at the initial examination and who are ultimately proven to have benign disease.

The avoidance of unnecessary biopsies and follow-up examinations is desirable from a simple economic point of view, but this importance is minimised when consideration is given to the mental trauma unnecessarily inflicted upon patients in these categories. There is inevitably scarring resulting from the surgical incision, which may be minimal in surgical terms but often assumes considerable significance to the patient. Moreover, there is an undoubted morbidity and even mortality associated with biopsies performed under general anaesthetic.

It is considered that if the specificity of mammographic interpretation was to be significantly improved, then there would be a greater degree of reliance on the results of mammography, with a resultant reduction in the number of unnecessary biopsies.

For these reasons it was decided to ascertain whether the specificity of mammography could be improved with the aid of a computer. The first step was to study the relative importance of mammographic signs using a computer database. As a second-stage investigation, the database will be used in a prospective study to predict the benignity or malignancy of breast lesions prior to biopsy.

This paper describes only the first part of this project.

## BACKGROUND

The local current clinical practice is to biopsy all palpable lumps, aspirating cysts and obtaining a histological diagnosis on solid lesions. These procedures are undertaken irrespective of mammographic findings and, on occasion, without referral for mammography.

Between 2500 and 3000 mammographic examinations are performed in Nottingham each year, patients being referred for mammography from symptomatic breast clinics and from an open clinic associated with the DHSS trial of early detection of breast cancer by self-examination (UK Trial of Early Detection of Breast Cancer Group, 1981).

When mammography is performed the radiological opinion is routinely classified on a five-point scale, each of which carries a recommendation for action (Table I). Biopsy is always undertaken when recommended on mammographic grounds.

## MATERIALS STUDIED

Patients are entered into this study on the basis that a biopsy has been performed and a histological diagnosis obtained during the course of management, with mammography performed within 1 month prior to biopsy. For the purpose of the study, all mammograms are re-examined without knowledge of the biopsy outcome

This paper reports on the first 500 patients. Of these, 260 had cancer and 240 benign disease. The indications for biopsy are given in Table II, which illustrates the need for improvement in the selection of patients if women with benign disease are to avoid biopsy. Certainly, simple clinical selection is poor in this series, the best (highest cancer rate) being selection following combined clinical and mammographic evaluation.

TABLE I

THE CLASSIFICATION OF MAMMOGRAM CONCLUSIONS AND THE MANAGEMENT RECOMMENDATION RESULTING FROM THESE

| Mammogram conclusion | Management recommendation |
|---|---|
| 1 Malignant<br>2 Probably malignant | Biopsy |
| 3 Indeterminate<br>4 Probably benign | Clinical review at 6 weeks, 2 months and 6 months. Further mammography at 6 months |
| 5 Benign/no lesion | No action |

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*Requests for reprints.

TABLE II

INDICATIONS FOR BIOPSY*

| Indicator | No. of patients | | |
|---|---|---|---|
| | Totals | Biopsy | |
| | | Malignant | Benign |
| Mammogram | 200 (40%) | 140 (70%) | 60 (30%) |
| Clinical | 195 (39%) | 35 (18%) | 160 (82%) |
| Both | 105 (21%) | 85 (81%) | 20 (19%) |
| Totals | 500 | 260 | 240 |

*Five hundred biopsied patients, all of whom had both clinical and mammographic examination, analysed on the basis of the modality which indicated a need for biopsy.

This paper concentrates on the identification of discriminating mammographic signs and their use in diagnosis. A similar investigation into specific clinical signs is planned to be the subject of a future study.

### RETROSPECTIVE ANALYSIS

On the basis of previous experience, specific radiological features were first identified as likely to be of value in the discrimination between malignant and benign disease. These features were grouped so that three patterns could be characterised for each patient: one for any lesion present, a second for the reaction to a lesion and the third for any calcification detected (Table III).

For each patient these features, together with patient identification data and histological details determined following biopsy, were entered into a database on a BBC microcomputer with a Torch disk pack.

The relationship identified in these patients between the presence of each individual mammographic sign and malignancy is shown in Fig. 1. One particularly interesting feature has been identified with regard to the subcutaneous reaction. Although in this series, which because of the selection criteria contained no patients with systemic problems or inflammatory breast disease, this sign had a low incidence (17%), when present it had a very high specificity (96%) as a cancer marker. This has been reported in detail in a separate communication (Roebuck, 1984).

In order to establish the relationship of each mammographic sign to a malignant outcome, the data were transferred to a mainframe computer and a stepwise discriminant analysis performed using the BMDP statistical package (Dixon et al, 1983). In order to implement this, some related mammographic

TABLE III

RADIOLOGICAL FEATURES*

| Lesion pattern | Reaction pattern | Calcification pattern |
|---|---|---|
| L1† Lesion detected | R1† Reaction | C1 Calcification |
| L2† Dysplasia only | R2 Oedema | C2† High density |
| L3 Homogeneous texture | R3 Diffuse density | C3† Size, predominantly small, < 1 mm |
| | | C4 Size, predominantly medium, 1–2 mm |
| L4† Density greater than gland tissue | R4 "P" reaction‡ | C5 Size, predominantly large, > 2 mm |
| L5 Density equal to gland tissue | | |
| L6 Density less than gland tissue | R5† Subcutaneous reaction | C6 Size, all equal |
| L7† Margins well defined | R6 Local skin thickening | C7 Shape, round |
| L8 Margins segment ill defined | | |
| L9 Margins ill defined | R7† Periareolar skin thickening | C8 Shape, rods |
| L10† Spicules present | | C9 Shape, irregular |
| | R8 Distant skin thickening | |
| L11 Comet tail present | | C10 Shape, mixed |
| | R9 Hypervascularity | |
| L12 Size less than 1 cm | | C11 Position, clusters§ |
| L13 Size more than 1 cm | R10 Parenchymal deformity, pulled | |
| | | C12† Position, rows |
| | R11† Parenchymal deformity, pushed | C13 Position, scattered |
| | | C14 Number, five or less |
| | | C15 Number, more than five |

*The radiological features grouped into the three categories. For discriminant analysis the bracketed features were considered to be related and those marked with a dagger were found to be the more important.

‡A reaction characterised by prominence of duct shadows, usually extending from the region of the lesion to the nipple.

§Contained within an area of diameter 1 cm

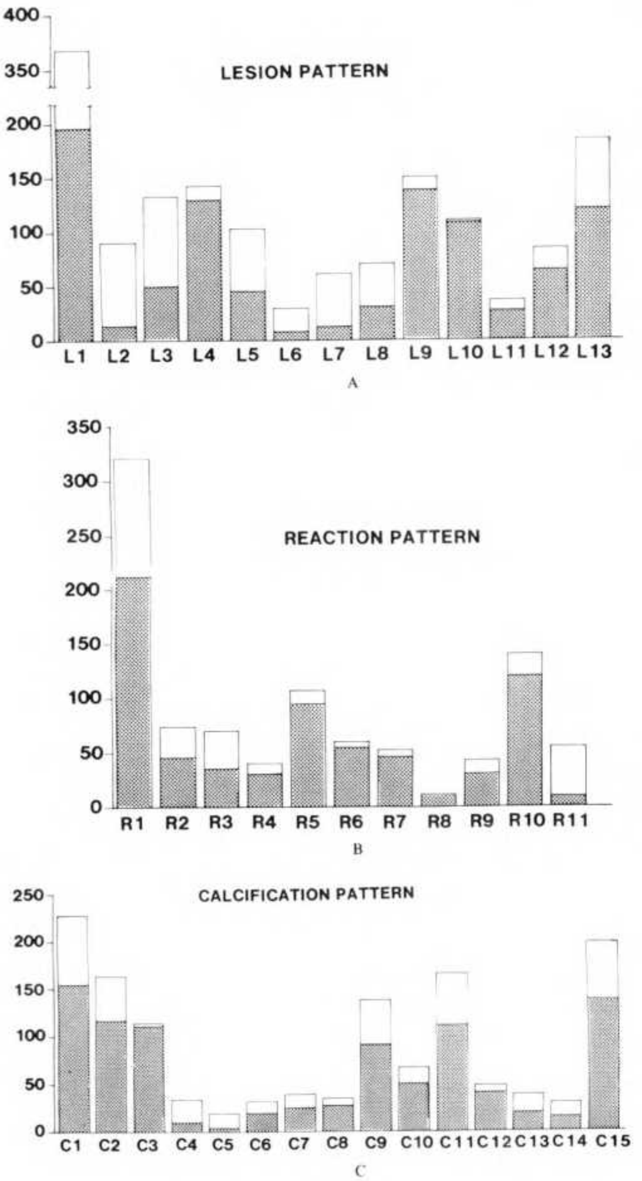

FIG. 1.

Incidence of each radiological feature (unshaded) and its relationship to malignant outcome (shaded). See Table III for feature details.

features, such as the degree of definition of the margins of a lesion, were treated as various levels of the same feature (see Table III).

The initial discriminant analysis identified nine of the features tested as important in distinguishing between a benign and a malignant outcome. Statistical cross-validation demonstrated that an additional three features should be considered and the final discriminant analysis employed the 12 features shown in Table III.

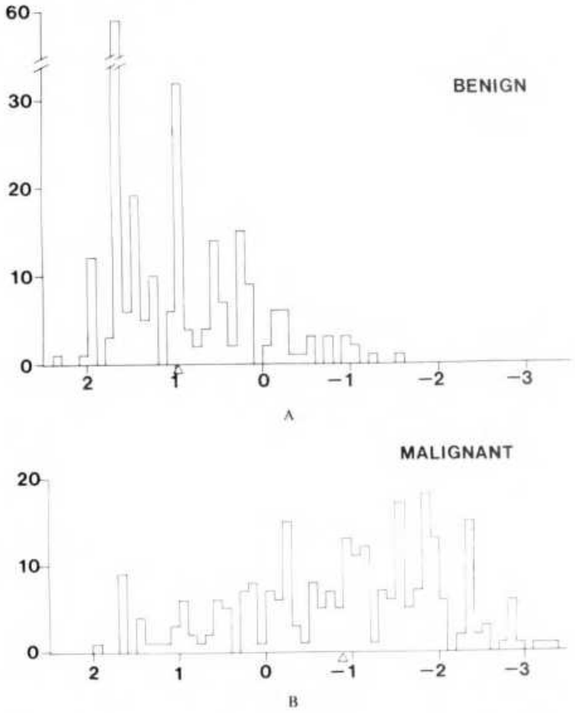

FIG. 2.

Distribution of all 500 cases on the canonical variable. The cases are classified according to their histological report. Any case having a negative value was reported by the computer program as malignant and any positive value was considered benign. Mean value of each distribution is represented by a triangle.

The discriminating features identified by this analysis were then applied to each individual case, in order to establish the probability of a correct prediction of a benign or a malignant outcome based solely on the presence or absence of these specific radiological features. A computer program was then written which used these features in an algorithm, and this was found to predict correctly 78% of the malignant and 88% of the benign cases. This is shown in Fig. 2, where all 500 cases are plotted on the variable which discriminates most between the two groups (*i.e.* the canonical variable; Dixon et al, 1983). Reasonably good separation of the benign and malignant groups is demonstrated, with a central overlap of cases which could be classified as mammographically indeterminate.

This overlap might be anticipated since the database information is entirely dependent on the accurate identification and interpretation of the mammographic signs. Visual examination of radiographs is always subject to error, error rates as high as 30% having been reported in various series (Gale et al, 1979).

The original (pre-biopsy) radiological opinion and the computer prediction were then compared to the

TABLE IV

COMPARISON OF RADIOLOGIST'S AND MAMCAD PREDICTIONS*

| Biopsy | Radiologist | | | | | | | MAMCAD | | | | Totals |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Malignant | | Indeterminate | | Benign | | NA | Malignant | | Benign | | |
| | No | % | No. | % | No | % | No | No | % | No. | % | |
| Malignant | 212 | 87.2 | 18 | 7.4 | 13 | 5.4 | 17 | 203 | 79 | 57 | 21 | 260 |
| Benign | 73 | 33.5 | 38 | 17.4 | 107 | 49.1 | 22 | 29 | 12.4 | 211 | 87.6 | 240 |
| Totals | 285 | | 56 | | 120 | | 39 | 232 | | 268 | | 500 |

*Radiologist's original, pre-biopsy, opinion and program predictions of outcome for the series of 500 cases. Thirty-nine of the original radiological reports were not available (NA) and these cases were omitted in calculating the percentage values for each cell. The indeterminate cases were recommended for follow-up.

final histological diagnosis. The results are shown in Tables IV and V.

Disregarding the 39 cases for which no original radiological diagnosis was available, a significant difference was found between the radiologist's original, pre-biopsy opinion and the computer program's prediction of malignant outcome ($\chi^2 = 12.9$, $p < 0.001$). For the residual 461 cases the incidence of true positive diagnoses of cancer by the radiologist (87.2%) was better than that of the feature-identification approach (79%). However, this was accompanied by an increase in the incidence of false positive diagnoses, the radiologist having a rate of 33.5% and the latter only 12.4%.

When the predictions for benign disease are examined, again a significant difference is found between the computer program and radiologist ($\chi^2 = 5.1$, $p < 0.05$). The radiologist made 49.1% true negative decisions for benignity and 5.4% false negatives. In contrast, the feature-identification approach predicted the benign outcome correctly in some 87.6% of cases, although this was accompanied by an increased false negative rate of 21%.

In terms of patient management, had the "feature identification" diagnosis been the sole criterion for biopsy, 268 fewer biopsies would have been undertaken overall. Unnecessary biopsies (*i.e.* those on benign disease) would have been reduced by 211 and 104 additional patients would have been correctly reassured that their disease was benign, as compared with what had happened in practice, where only 107 true benign cases were reported.

The disadvantage of the prediction based on presence of features lies in the increased false negative rate. Ignoring those cases where the original radiological report was unavailable, this approach recommended that 51 cancer patients be discharged whereas the original radiologist had recommended discharge of only 13 such patients. This difference is largely accounted for by the radiologist's ability to recommend follow-up in 18 cases, a facility not so far incorporated into the feature approach in this study.

It can be seen that there is a bias in the radiologist's recommendation towards biopsy. This is not unexpected in view of the natural inclination to "play safe". In the correction of this bias the feature approach "refused" biopsy in 36 patients with cancer which were appropriately reported by the radiologist, and "missed" eight cancers which the radiologist might have detected on follow-up (These cases were, in fact, biopsied on clinical grounds.)

### COMPUTER-ASSISTED DIAGNOSIS

Following these encouraging results it was decided to initiate a prospective study which would assess the effect of having a computer prediction of benignity or malignancy available at the time of the initial mammogram interpretation.

A Mammographic Computer Assisted Diagnosis (MAMCAD) program has been designed which incorporates a database containing the previously described patient data. For each new case the patient identification data and the radiological features present on the mammogram are entered by the observer into the microcomputer at the radiologist's reporting station. The radiologist then enters the diagnosis he considers most likely on the basis of his experience. The program immediately responds with its predicted diagnosis, based on the previously described discriminant analysis. It then asks the observer if he wishes to alter his opinion and, if so, he enters the amended mammographic diagnosis. The patient information is

TABLE V

COMPARISON OF RADIOLOGIST'S AND MAMCAD PERFORMANCE (%)*

| | Radiologist | MAMCAD |
|---|---|---|
| Sensitivity | 87 | 79 |
| Specificity | 49 | 88 |
| Positive predictive value | 74 | 88 |
| Negative predictive value | 89 | 79 |

*In calculating these performance measures the 39 cases where the original radiologist's diagnosis was unavailable were omitted.

next transferred automatically to the database If a biopsy is subsequently performed the histological data are added at a later date. In this way the database is constantly updated as new cases are presented The purpose of this approach is that, as the database is expanded (and currently this contains data on 650 patients), additional good discriminating features or combinations of features may be identified. The facility to add to or replace the radiological features currently used in the MAMCAD prediction has been provided.

## DISCUSSION AND CONCLUSIONS

Individual mammographic features have been considered previously (Moskowitz, 1983), but the importance of the present approach is that it assesses the contribution of each feature when others are also present.

An analysis of multiple signs undertaken by Stotboam failed to show any improvement in diagnosis (Rombach, 1983). There was, however, a difference in approach in that Stotboam employed a multivariate cluster analysis technique.

These analyses have been undertaken on a specific group of individuals and the technique, although promising, is still unproven with respect to the complete spectrum of cases referred for mammography. However, it will be necessary to await fuller results from the prospective trial which is in progress, and to undertake a statistical analysis of practice with and without the use of MAMCAD program before a wider application of the technique can be recommended. The preliminary results are very encouraging and it does appear that the use of a MAMCAD program may enable a marked improvement in the specificity of mammographic diagnosis to be made.

## ACKNOWLEDGMENTS

We thank Professor R. W Blamey for access to clinical data, the Special Trustees for Nottingham University Hospitals for financial support, and Mrs D E. King for secretarial assistance.

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# Book reviews

*Ultrasound Diagnosis in Obstetrics and Gynecology.* Ed. by M. Hansmann, B-J Hackelöer and A Staudach, pp. xviii+495, 1985 (Springer-Verlag, Berlin), DM280.
ISBN 3-540-15348-9 (Berlin)
0-387-15348-9 (New York)

Not another textbook of ultrasound in obstetrics and gynaecology! There are so many all churning out the same information, often out of date by the time it is published This book, however, is different enough to make it stand apart from the rest Not only does it describe the current state of the art well and comprehensively, it also gives a good critical appraisal of the literature on each subject. It does not ignore problem areas or, worse, deal with them in a dogmatic fashion; instead it sets out the problem and looks critically at the various solutions.

The book covers all aspects of obstetrics and gynaecology; there is even a chapter on breast ultrasound The main emphasis is, however, on the second and third trimesters of pregnancy and fetal biometry and abnormality There are of course the obligatory chapters on physics, instrumentation and safety.

The book will appeal to, and be of value to, all practitioners and users of obstetric and gynaecological ultrasound. For the beginner it does not irritatingly assume an unrealistic basic level of knowledge, but carefully explains the fundamental concepts and techniques. Important, everyday procedures such as the correct way to measure a biparietal diameter, just how to manipulate the probe to obtain the anatomical views required, all are carefully explained. For the more experienced and those responsible for organising an ultrasound service, all the ultrasound applications in obstetrics and gynaecology are carefully evaluated; for example, in the chapter on gynaecological pathology, instead of merely listing the ultrasound appearances in each particular disease process the role of ultrasound is discussed in relation to its lack of specificity in gynaecological pathology. Again, in the discussion on fetal growth, the numerous parameters available are not only described but their relative merits are also assessed. The problem of screening programmes in obstetric ultrasound is addressed and although some of the discussion is not relevant because it relates to the system of health care in West Germany there are many common problems. Of particular value to those working on their own is the critical appraisal of fetal biometry. In this field there is so much work published where conclusions are drawn from numerical data that it can be difficult for the non-statistician to evaluate The pointers given in this section will help the reader to recognise useful data from which relevant conclusions can be drawn

In any ultrasound text the illustrations are going to be of paramount importance In this book the quality of the images throughout is consistently high The majority of the images are real-time, thus avoiding the recent trend of singing the praises of real-time ultrasound in the text then illustrating it with images from static-image scanners Although the quality of the images is high, the annotation is somewhat confusing in places, but this is the only minor irritation in an otherwise superb book.

In conclusion then, it is an excellent textbook with wide appeal It would be extremely valuable as a bench-book in all obstetric ultrasound departments, large or small However, costing over £100, it is probably too expensive for the individual user

M GOWLAND

*Obstetric Ultrasound How, Why and When* By Patricia Chudleigh and J. Malcolm Pearce, pp. 194, 1986 (Churchill Livingstone, Edinburgh), £14.95.
ISBN 0-443-03163-0

This is an excellent short textbook written by two practitioners at King's College Hospital experienced in obstetric scanning, with a foreword by Professor Stuart Campbell.

It is a comprehensive, easy-to-read text dedicated solely to ultrasound in pregnancy. It covers adequately all the practical aspects of obstetric scanning with clear descriptions of normal and abnormal appearances Written by an ultrasonographer and an obstetrician, it succeeds in explaining the role of ultrasound by a knowledge of pregnancy and its problems The book is aimed at anyone doing obstetric ultrasound including radiographers, radiologists and obstetricians. It is particularly suited to those studying for the Diploma in Medical Ultrasound, with a high standard of description of techniques and adequate anatomy and pathology. Whilst most experienced radiologists would gain little additional information, it is, however, very appropriate for radiologists in training and undertaking the Fellowship examination

The layout is excellent, with a natural progression of chapters from normal appearances, complications in early pregnancy, estimation of gestational age, and fetal anomalies to normal and abnormal growth The concluding chapters include helpful advice on organising an ultrasound department to provide a routine service and straightforward basic physics, somewhat unusually at the back of the book. There are numerous diagrams and well labelled illustrations of a very high standard. Unfortunately, there are a number of minor but irritating spelling and grammatical errors scattered throughout the book.

However, this is an extremely useful text, up to date and good value in paperback at £14.95. It is a useful addition to the books already available and highly recommended in particular for training radiographers and radiologists

C HAYWARD

*A Practical Guide to Ultrasound in Obstetrics and Gynecology.* By E. E Sauerbrei, K. T. Nguyen and R. L. Nolan, pp. x+185, 1987 (Raven Press, New York), $28 50.
ISBN 0-88167-268-8

This book covers the most important areas in obstetric and gynaecological ultrasound in a compact format. It sets out to be a practical guide to both the normal and abnormal with helpful clinical comments as well as description and illustration of ultrasound appearances. The book is well laid out and the quality of the illustrations is excellent.

Inevitably in such a small volume there are omissions, but in particular it would have been useful to have a discussion of ultrasound in *in-vitro* fertilisation A bibliography would also have been useful to direct readers to more comprehensive discussions of some matters. There are some inaccuracies, in particular in the section on fetal abnormalities with misleading statements such as "There is nearly always bladder outlet obstruction . . " in prune-belly syndrome and, when discussing sacrococcygeal teratomas, "33% of cases are malignant ."

Overall the book is a very good compact guide to obstetric and gynaecological ultrasound and its "pocket" size should mean it is often referred to by radiologists in training and radiographers training in ultrasound. Its price, however, suggests that it will be purchased by very few of those for whom it is most suitable

D W. PILLING

1987, *The British Journal of Radiology*, *60*, 893–896 SEPTEMBER 1987

# Influence on patient management of general practitioner direct access to radiological services

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(*Received February 1986 and in revised form November 1986*)

## ABSTRACT

We have looked at the effect of open radiological access on patient management during a 2-year prospective study in the radiology department of a teaching hospital and two general practices. Five hundred and thirty consecutive requests for radiological examination were studied Chest radiographs (29 8%) and barium meals (17.4%) were the investigations most commonly requested. At the time of referral general practitioners indicated that if open radiological access had not been available, 78% of the patients would have been referred to specialist clinics. They also indicated that with a normal initial radiological examination only 12% would need referral to a specialist department. Open access appears to save outpatient consultations

Previous studies (Cook, 1966; Wright et al, 1979; Mills & Reilly, 1983) on the use of radiological services by general practitioners have concentrated on access, referral patterns, resultant workload for radiology departments and incidence of abnormality found. These studies document the general practitioner's use of the facilities, and some break down the type of investigation requested into contrast, non-contrast or chest radiograph, together with the age and sex of patient. Wright et al (1979), who studied 1394 consecutive patients, state that general practitioner referrals produce fewer repeat and follow-up requests, fewer multiple requests and a greater proportion of abnormal reports than referrals from outpatient clinics. Referrals from general practitioners were not precipitate and were often preceded by the appropriate clinical examinations. These authors conclude that open access has important benefits in conserving other hospital resources. The resulting radiological workload is discussed by Brindle (1978). Experience with a special X-ray unit for general practitioners is discussed by Davis and Williams (1968). The range of radiological facilities available to general practitioners is variable and often determined on a local basis. The Joint Working Party of the Royal College of Radiologists and the Royal College of General Practitioners in its Report on Radiological Services for General Practitioners (1981) recommended that general practitioners should have adequate diagnostic facilities available, and that direct access is essential.

Our prospective study aimed to assess the effect on the management of patients of allowing their general practitioners open access to a radiology department over 2 years. As well as documenting the number and type of investigations requested, we looked at the general practitioner's reasons for the requests, his alternative management if radiology were not available, and his prediction of the effect of positive or negative radiological findings on managing patients.

## METHOD

Two established group practices (each of six principals and one trainee), one in the centre of Cambridge and one in a nearby village, were invited to participate in the study. Over a 2-year period the practices were given complete access to the radiological facilities at Addenbrooke's Hospital, with the exception of computed tomography and angiography. (Nuclear Medicine, as a separate department, was not involved in this study.)

When making the radiological referral, the general practitioner completed a form recording the purpose of the investigation: whether to confirm the clinical diagnosis, exclude serious illness or reassure the patient. The general practitioner was also asked his alternative management if the investigation was not available, whether he would attempt to obtain the investigation elsewhere, to refer the patient to a specialist department, or begin active treatment. A further question required prediction of management in the event of the investigation confirming or excluding an expected abnormality, or confirming normal findings. The pattern of proposed follow-up was also recorded.

## RESULTS

Over the 2-year period 530 completed forms were analysed; 412 came from the city practice, 118 from the village practice. The relative frequency with which different investigations were requested is shown in Table I. The commonest working diagnoses are shown in Table II.

The reasons for referral were to confirm the clinical diagnosis in 47%, to exclude serious illness in 46% and

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*Present address: Department of Radiology, Hereford County Hospital, Hereford.

†Present address: Department of Radiological Sciences, Guy's Hospital, London.

TABLE I

REQUESTS FOR RADIOLOGICAL EXAMINATIONS

| Examination | % of total requests |
|---|---|
| Chest | 29.8% |
| Barium meal | 17.4% |
| Lumbar spine | 6.6% |
| Pelvis | 6.6% |
| Ultrasound | 6.4% |
| Cholecystogram | 6.0% |
| Knee | 4.3% |
| Ankle/foot | 3.6% |
| Skull | 2.8% |
| Cervical spine | 2.8% |
| Abdomen | 2.5% |
| Dorsal spine | 1.9% |
| Elbow | 1.9% |
| Wrist/hand | 1.9% |
| Tibia and fibula | 1.5% |
| Barium enema | 1.3% |
| Humerus | 0.9% |
| Femur | 0.9% |
| Mammogram | 0.6% |

TABLE II

PERCENTAGES OF COMMONEST WORKING DIAGNOSES FOR 530 RADIOLOGICAL EXAMINATIONS

| Diagnosis | % of total diagnoses |
|---|---|
| Peptic ulcer | 14.7% |
| Inflammatory chest disease | 13.5% |
| Neoplastic chest disease | 11.7% |
| Gallstones | 11.1% |
| Degenerative disease axial skeleton | 7.7% |
| Peripheral skeletal trauma | 5.1% |
| Hiatus hernia | 3.2% |

to reassure the patient in 7%. If the investigation had not been available, in 63% of cases the general practitioner would try to obtain it, either elsewhere or by referral through a hospital outpatient clinic, and in 37% he would not pursue the matter. Asked about referring the patient to hospital outpatient departments, the general practitioners' conclusions were 68% of patients with an expected abnormality confirmed would be referred; if an expected abnormality were excluded, 32% would be referred, and if no abnormality were detected, only 12% would be referred (Table III).

General practitioners were asked whether they would actively treat the patient if the test was not available (Table IV). The answer was "yes" in 56% of the cases. If an expected abnormality was confirmed by the investigation, 77% of such patients would be treated by the practitioners, and 74% treated if the expected abnormality was excluded. Of patients without confirmation of abnormality, 63% would still receive treatment.

If the tests were unavailable or confirmed the expected abnormality, then the median time to the patient's next appointment with the practitioner would be 2 weeks (Table V). If the expected abnormality were excluded or if no abnormality was confirmed, the median time to the next appointment would be 3 weeks. Table VI shows that between 58% and 69% of radiographs were of help in management decisions and that negative, as well as positive, results were thought useful.

## DISCUSSION

Chest radiographs and barium meals were the commonest request (Table I), the number of chest radiographs was probably underestimated as there is direct access to an "X-ray only" clinic in our chest clinic. Our referring general practitioners like to have a diagnosis of peptic ulcer confirmed before treatment, but have no direct access to endoscopy services in this hospital. However, Mills and Reilly (1983) state that in their study the majority of examinations requested by three of the four practices were of the skeleton, and not chest radiographs or contrast studies Our ultrasound examinations (virtually all for the gallbladder) and oral cholecystogram requests were approximately equal, at 6.4% and 6.0% respectively, indicating acceptance of ultrasound reports by the general practitioners for gallbladder disease.

The few requests for barium enemas (seven (1.3%) in 2 years) and none for intravenous urograms (IVUs) reflect the fact that in this hospital there is generally no open access for these investigations and, thus, general practitioners are not familiar with requesting them. A total of 93% of our requests were to confirm a suspected clinical diagnosis or to exclude serious illness; surprisingly, only 7% were requested to reassure the patient. In contrast, Mills and Reilly (1983) state that in their study most radiographic examinations were used

TABLE III

OUTPATIENT REFERRALS IN RELATION TO RADIOLOGY RESULTS

| | If test were not available | If test *confirms* expected abnormality | If test *excludes* expected abnormality | If test *confirms* no abnormality |
|---|---|---|---|---|
| Would GP arrange hospital appointment? | | | | |
| No | 22% | 32% | 68% | 88% |
| Yes | 78% | 68% | 32% | 12% |

TABLE IV

PROPOSED TREATMENT IN RELATION TO RADIOLOGY RESULTS

| | If test were not available | If test *confirms* expected abnormality | If test *excludes* expected abnormality | If test *confirms* no abnormality |
|---|---|---|---|---|
| Would patient be actively treated? | | | | |
| No | 44% | 23% | 26% | 37% |
| Yes | 56% | 77% | 74% | 63% |

TABLE V

PROPOSED FOLLOW-UP IN RELATION TO RADIOLOGY RESULTS

| | If test were not available | If test *confirms* expected abnormality | If test *excludes* expected abnormality | If test *confirms* no abnormality |
|---|---|---|---|---|
| Median time to next appointment | 2 weeks | 2 weeks | 3 weeks | 3 weeks |

TABLE VI

VALUE OF RADIOLOGY RESULTS IN RELATION TO MANAGEMENT

| | If test were not available | If test *confirms* expected abnormality | If test *excludes* expected abnormality | If test *confirms* no abnormality |
|---|---|---|---|---|
| Is radiology result valuable in making management decisions? | | | | |
| No | — | 37% | 42% | 31% |
| Yes | — | 63% | 58% | 69% |

to exclude rather than confirm abnormality, with over 85% of results confirming the general practitioner's initial assessment. We asked general practitioners what they would do if the investigation they wanted was not available. In only 63% of cases would they explore other possibilities of obtaining the investigation: it is relevant that at our hospital general practitioners have, for many years, had access to all investigations except IVUs, barium enemas, angiography and computed tomography. This is not always so in other centres, although recommendations on access to diagnostic facilities have been made in the Joint Working Party Report on Radiological Services for General Practitioners (1981)

Even with available diagnostic facilities, referral patterns differ widely between doctors (Macaulay, 1962). While our study does not take into account referral rates from the two practices, a study from Aberdeen (Mair et al, 1974) showed a variation of between 0 and 200 referrals per 1000 patients per year. Older doctors refer fewer patients than younger (Morrison & Riley, 1963; Davis & Williams, 1968) and part-time general practitioners refer more patients than full-time ones (Mills & Reilly, 1983). If the tests were not available, 78% of patients would have been referred for an outpatient appointment; this referral rate dropped to 12% when there was no abnormality found Thus, in this study there has been a considerable saving in outpatient referrals. This has to be balanced against an increased workload for the radiology department While the workload for radiology departments is increasing (Brindle, 1978), between 1958 and 1977 the proportion of general practitioner requests was constant (Lennon, 1969; Macaulay, 1962; Freeman, 1983). It is likely that open access to the radiology department will result in a considerable amount of time being saved, for both the patient and the general practitioner, in resolving the diagnostic problem. Access to radiological facilities does not really change the proportion of patients actively treated, but the treatment might be more appropriate. Casualty experience shows the initial diagnosis is altered by radiology in only 16% of cases (Loop & Lusted, 1978). General practitioners regard radiology reports as having a direct effect on patient management in 22–36% of cases, a normal report being as helpful as an abnormal one (Mills & Reilly, 1983)

We conclude that in our setting, open access to radiological facilities for general practitioners results in a considerable reduction in numbers referred to hospital outpatients. It has little effect on the proportion being actively treated. It is important to bear in mind that patients referred for X-ray examinations are likely to be referred to hospital. Direct access lightens the load and makes referrals more appropriate when made. However, radiology departments can provide this service only if adequately provisioned with equipment and staff.

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1987, *The British Journal of Radiology*, 60, 897–906 SEPTEMBER 1987

# The Sheffield stereotactic radiosurgery unit: physical characteristics and principles of operation

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(*Received September 1986 and in revised form January 1987*)

ABSTRACT

A stereotactic radiosurgery unit was commissioned in Weston Park Hospital in the summer of 1985. This paper describes the design, principles of operation and the safety features of the multiple-beam cobalt-60 therapy unit The measurement of the dose around the extremely sharp focus produced by the 201 beams is discussed and the results compared with computed distributions The results of the radiation protection survey are presented and the design of the purpose-built treatment suite is discussed The procedure for treatment of a patient is outlined.

Stereotactic radiosurgery was developed to facilitate the treatment of deep-seated lesions in the brain, inaccessible to conventional neurosurgical techniques.

Leksell (1951) used a stereotactic apparatus for the localisation of a lesion and also to control the direction of a series of narrow beams of 200 kV X rays which were used to irradiate it. Irradiation from a number of different angles produced a focal effect at the lesion and thus treatment was effected with minimal dose to the surrounding tissue. Appreciating the limitations of the low-energy X rays, the Leksell group proceeded to investigate the use of high-energy proton beams (Larsson et al, 1958), a technique which has been further developed and applied clinically by Kjellberg et al (1977) and Fabrikant et al (1984). However, Leksell (1968) found the synchrocyclotron too complicated for general neurosurgical use and developed a dedicated multiple-beam cobalt-60 therapy unit. This facilitated the simultaneous irradiation of a lesion by 179 cobalt sources, which were distributed in a fixed hemispherical pattern. Each source produced a finely collimated gamma-ray beam which was directed towards a common focal spot (the centre of the hemisphere). The combination of all the sources resulted in a well defined focus of high dose with a rapid fall-off of dose with distance from the edge of the irradiated volume.

The radiosurgery unit in the Karolinska Institute in Stockholm has been used for the treatment of a wide range of brain disorders. Leksell (1968) initially described the treatment of intractable pain by thalamotomy. More recently, Backlund et al (1972, 1974; Backlund, 1979) have used the technique for hypophysectomy and for the treatment of pinealoma and craniopharyngioma. Other pituitary conditions, including Cushing's syndrome (Thoren et al, 1978) and pituitary adenoma (Rahn et al, 1979), have been treated and Steiner et al (1977) have reported that radiosurgery is efficacious in the obliteration of cerebral arterial malformations.

In November 1984 the Department of Health purchased for evaluation a radiosurgery unit of similar design to that used by Leksell in Stockholm. It has been installed in an extension to the Radiotherapy Department of Weston Park Hospital, Sheffield. Installation was completed in July 1985. The unit will be evaluated over a period of 5 years in a research programme conducted by the Departments of Neurosurgery, Radiotherapy and Medical Physics. The patients to be treated will be drawn from centres throughout the United Kingdom.

The purpose of this paper is to describe the principles of operation and physical characteristics of the treatment unit. The clinical results will be the subject of a later report.

## TREATMENT UNIT

The radiosurgery unit (Bradshaw, 1986) was manufactured by Nucletec SA (Switzerland) (a subsidiary of Scanditronix AB, Sweden) and is shown in Fig. 1. The central body of the unit is a steel casting and incorporates 201 separate and individually collimated cobalt-60 sources which are mounted in a hemispherical source housing. A single shutter, situated at the front of the central body, provides protection from the radiation while the unit is not in use and can be opened to facilitate access to the irradiation area.

A patient couch is situated in front of and accurately aligned to the central body. Secondary collimation is contained within a hemispherical steel helmet which is mounted at the head of the couch (Fig. 2A).

During treatment the patient's head is secured within the helmet in such a position that the lesion to be treated is at the centre of the hemisphere. The shutter is then opened and the patient couch is driven, under hydraulic control, into the central body. Irradiation of the lesion commences only when the primary and secondary collimators align (Fig. 2B) at the end of the travel. Microswitches confirm the correct positioning of

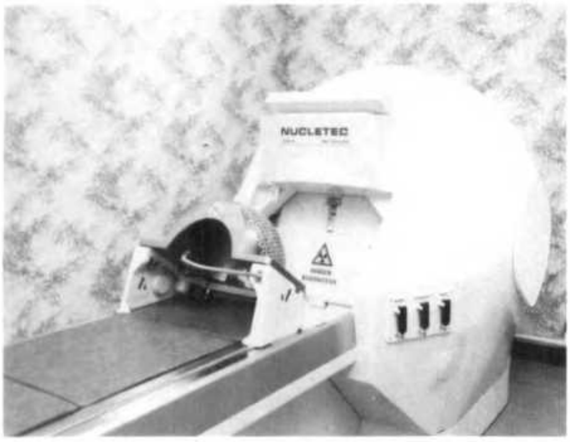

Fig. 1.
The stereotactic radiosurgery unit.

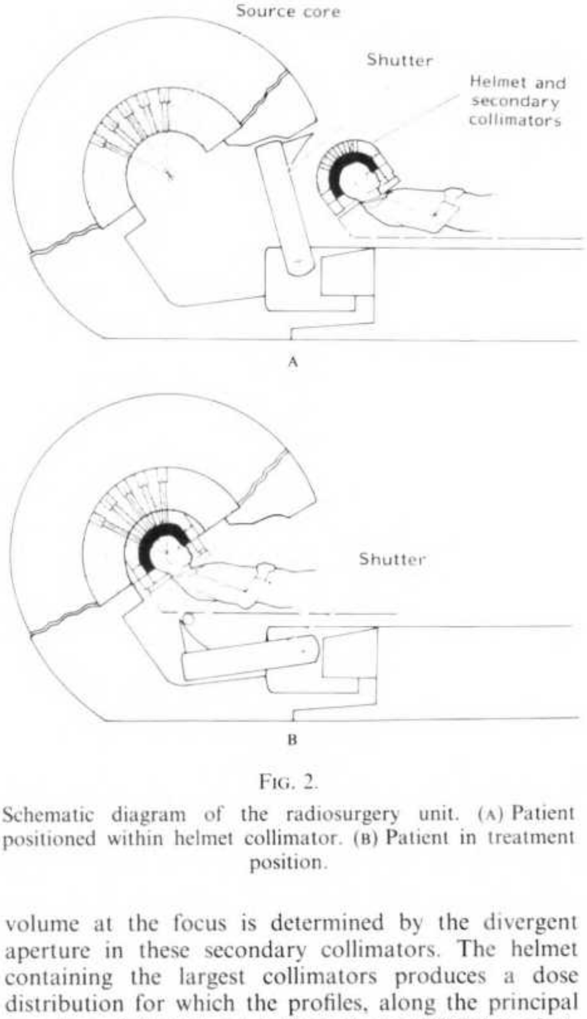

Fig. 2.
Schematic diagram of the radiosurgery unit. (A) Patient positioned within helmet collimator. (B) Patient in treatment position.

the helmet in relation to the source core and terminate the treatment if the helmet moves more than 0.1 mm.

*Sources and collimation*

The cylindrical sources of cobalt 60 are each 1 mm in diameter and 20 mm long. They are constructed from 20 pellets of cobalt in tandem and doubly encapsulated in stainless steel. Each source is further contained within a source pencil, which serves to secure and align the source to the collimation system. The sources had a nominal activity at the time of delivery of 1.04±0.03 TBq (28 Ci), the total activity in the unit being 209 TBq (5500 Ci). The sources are distributed evenly over a 160°×60° sector of the hemispherical source core (Fig. 3). This is a steel casting which is precisely machined such that the beam from each source is directed towards the focus. The tolerance in the direction of each beam channel was ±0.015°, which would result in a maximum misalignment at the focus of ±0.1 mm.

The beam from each source is collimated over a total length of 185 mm to produce a fine beam of gamma rays. Figure 4 shows the source, source pencil, collimator tube and tungsten collimators. Primary collimation is achieved in two stages. The first collimator is 30 mm in length and has a cylindrical aperture. The second is 95 mm long and has an aperture which diverges from a 3.6 mm to a 7.2 mm diameter. These primary collimators are secured together with the source in a collimator tube which is mounted within the source core.

The final collimation is produced by selection of one of three helmets. These can be removed from the patient couch and interchanged using a mechanical hoist. Each helmet contains 201 tungsten collimators, which are precisely positioned such that they will align with the primary collimators when the couch reaches the treatment position. The size of the irradiated volume at the focus is determined by the divergent aperture in these secondary collimators. The helmet containing the largest collimators produces a dose distribution for which the profiles, along the principal axes, have full widths at half maximum (FWHM) of 14, 18 and 20 mm. This is referred to as the "14 mm"

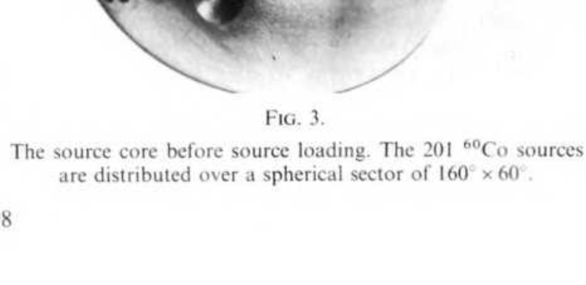

Fig. 3.
The source core before source loading. The 201 $^{60}$Co sources are distributed over a spherical sector of 160°×60°.

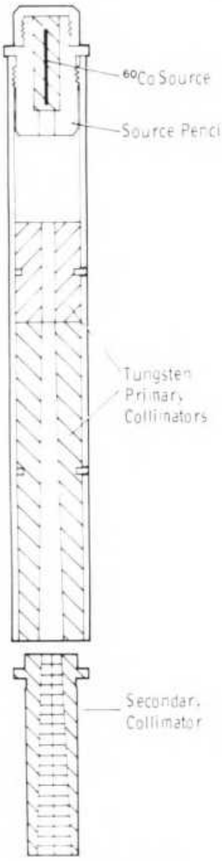

FIG. 4.

The arrangement of $^{60}$Co source, source pencil, primary and secondary collimators.

helmet. The "8 mm" and "4 mm" helmets produce distributions for which the FWHM values are 8, 9, 11 mm and 4, 5, 6 mm respectively.

Figure 5 shows physical models constructed to represent the shape of the volume contained within the 50% isocontours generated by the 4, 8 and 14 mm collimator helmets, while Fig. 6 shows two of the principal planes of the isodose distribution, produced at the centre of a hemisphere by the 14 mm helmet.

*Shielding and radiation protection*

The central body and the shutter of the unit were designed to reduce the leakage of radiation to acceptable levels as specified by the Code of Practice (Her Majesty's Stationery Office (HMSO), 1972). The Code of Practice does not directly relate to a treatment unit of this type but the principles were interpreted and applied wherever possible.

The central body consists of two halves. The lower part forms the base of the unit with sides and floor of steel to attenuate the primary beams and scattered radiation from the sources. The upper part is a hemispherical steel dome of 370 mm thickness which covers the source core and is bolted to the base. The joint between the upper and lower sections is staggered in 20 mm steps to minimise the leakage through the joint. The shutter, manufactured from cast iron, is 140 mm thick.

Figure 7 shows the results of the protection survey carried out on the central body of the unit. Several

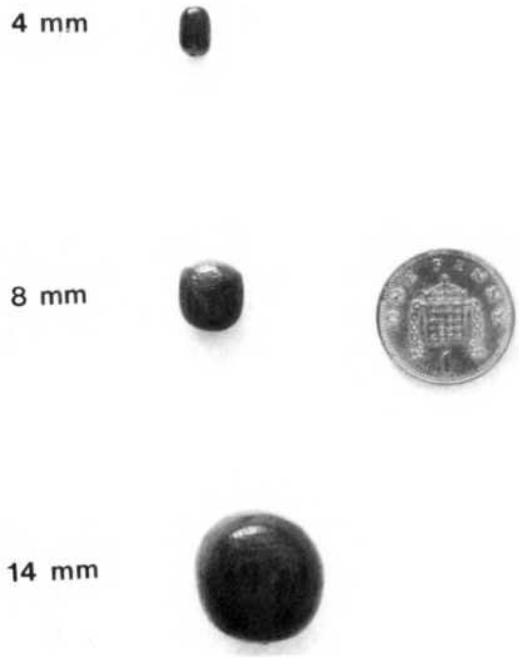

FIG. 5.

Physical models constructed to represent the volume contained within the 50% isocontours, generated at the focus of the 201 beams by the 4, 8 and 14 mm collimator helmets.

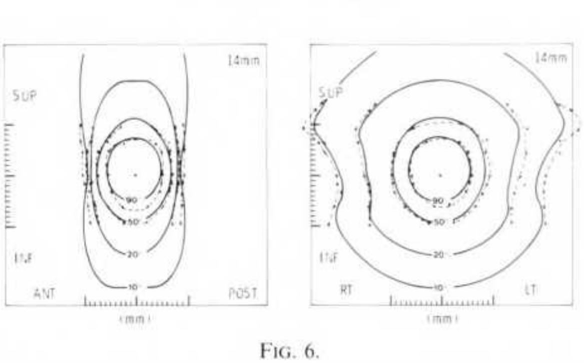

FIG. 6.

Measured and calculated isodose distributions obtained in two of the principal planes at the focus of the 14 mm collimator helmet.

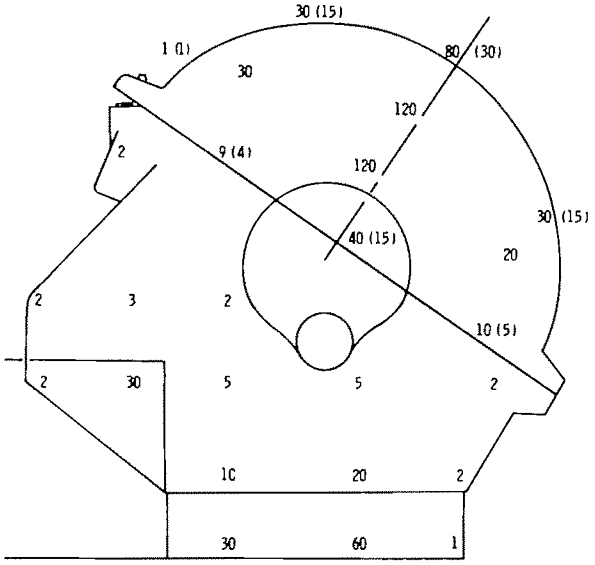

FIG 7.

Dose rate in $\mu$Sv h$^{-1}$ at 50 mm from the surface of the radiosurgery unit. Values in parenthesis are at 700 mm from the surface, *i.e.* 1.07 m from the nearest source.

points were found to be inadequately protected, one of which was at the joint between the two sections; the others were mainly associated with bolt holes. Additional protection was added to these points to reduce the leakage to acceptable levels. The values quoted are post-modification. Values in parenthesis are at 700 mm from the surface of the unit, *i e.* 1.07 m from the nearest of the 201 sources.

Dose rates at points close to the front of the shutter were slightly higher than the levels specified in the Code of Practice, rising to a maximum of 350 $\mu$Sv h$^{-1}$. This was associated with a bolt hole that could not be readily modified.

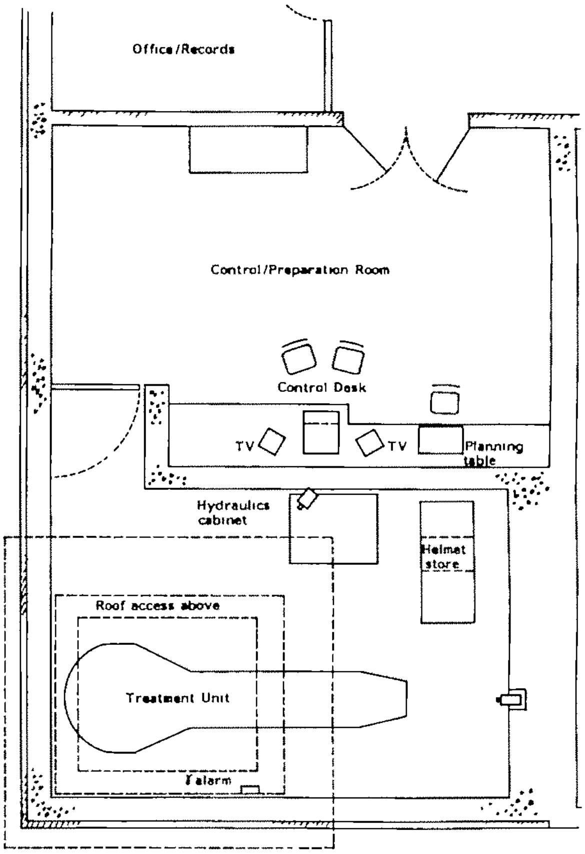

FIG 8.

The Radiosurgery Suite, Weston Park Hospital, Sheffield

## THE TREATMENT SUITE

The radiosurgery unit is housed in an extension to the Radiotherapy Department at Weston Park Hospital,

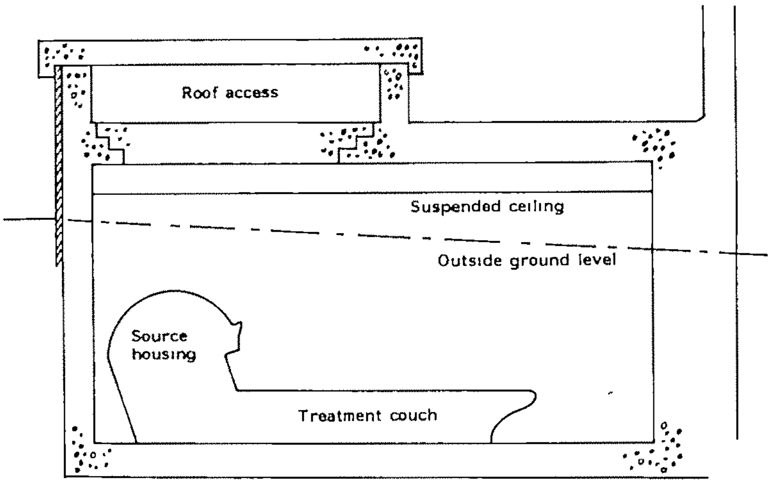

FIG 9.

The Radiosurgery Suite (elevation), Weston Park Hospital, Sheffield.

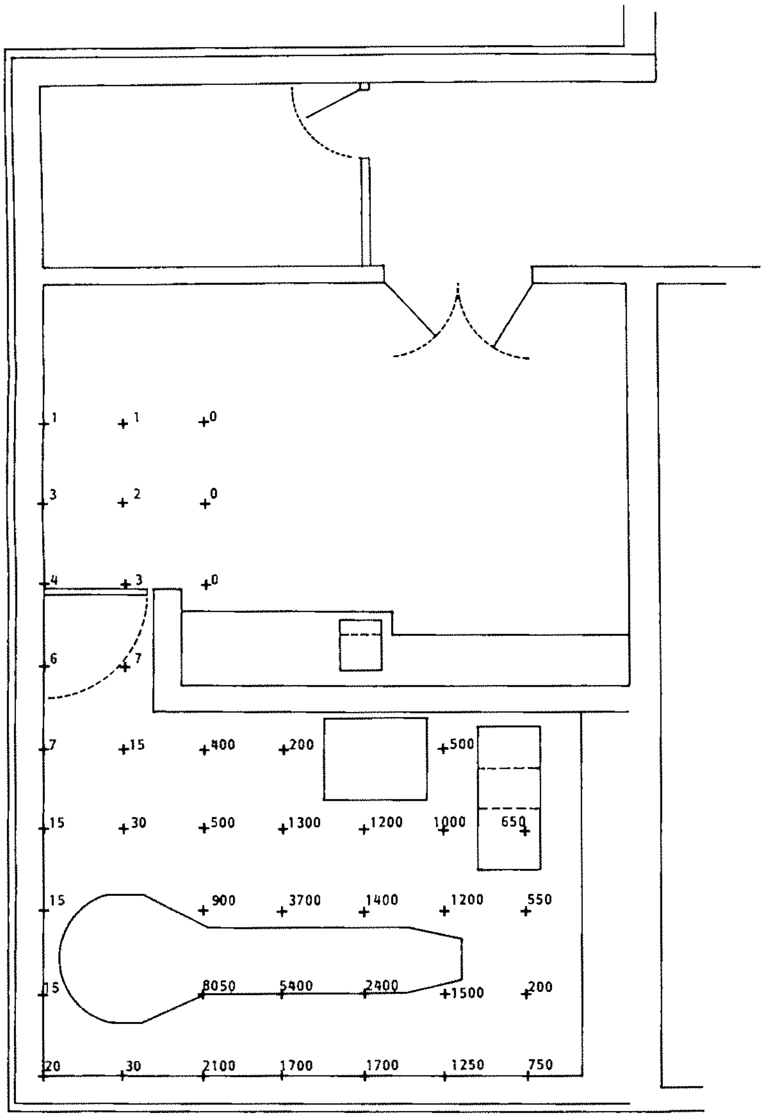

Fig 10.
Radiation field in $\mu$Sv h$^{-1}$ in the treatment room (1 m above the floor) with the 14 mm helmet *in situ*

which incorporates a treatment room, a control/preparation area and a small office (Fig. 8).

A particular feature of the suite is the roof access (Fig. 9). The weight of the unit is approximately 18 tonnes, largely concentrated in the source housing which will have to be removed from time to time to be fitted with new sources. Ease of access and of alignment with the rest of the equipment was therefore an important consideration in the design of the accommodation. With the treatment room half below ground level and with road access on two sides, the source housing can be delivered to the site and lowered through the roof into position using a mobile crane.

The guidance on the radiation protection of gamma-ray beam units in the Code of Practice (HMSO, 1972) and RASMP/75 (DHSS, 1975) was applied, in so far as it could be interpreted, to the design requirements of this equipment and to the suite of rooms. The uniqueness of the equipment lies in the large number of sources distributed over a spherical sector of 160° × 60° but without a "useful beam" emerging from it. All 201 primary beams are attenuated by the source housing itself after passing through the patient. The treatment room itself is required, therefore, only to attenuate further the leakage radiation from the source housing and the scattered radiation emerging through the open shutter aperture. The former is largely catered for by the inverse square law attenuation while the latter is of lower photon energy and relatively low intensity. Figure 10 shows the intensity distribution 1 m above the floor when the shutter is open with the 14 mm helmet *in situ*, within the treatment room and through the open maze

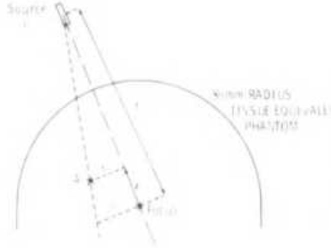

FIG. 11.
Calculations of the focal dose distribution assume that the focus of the beams is at the centre of a hemispherical phantom of tissue-equivalent material.

entrance. The entrance is protected by an interlocked bar gate.

The room design was largely based on data made available by the Karolinska Institute, Stockholm, which related to their own unit. The Sheffield unit was of a different design and, while some improvements had been incorporated, there were no guarantees of their effectiveness. In particular, the design sought to correct two relatively intense leakage paths through the edges of the open shutter. It was with this in mind that a thicker wall was specified to the foot of the couch to match the oblique thickness of the side walls. The thicker wall separates the treatment room from the existing hospital accommodation. The other three walls are 350 mm of 2.4 $\mathrm{t\,m^{-3}}$ concrete reinforced to support the adjacent roadway. These proved adequate, with no dose-rate measurements outside the external walls greater than 0.1 $\mu\mathrm{Sv\,h^{-1}}$ with the 14 mm helmet in the treatment position. The maximum dose rate measured on the control/preparation room wall was 0.4 $\mu\mathrm{Sv\,h^{-1}}$ and confined to a small area.

### BEAM MEASUREMENTS AND CALIBRATION

#### *Calculation and verification of the focal dose characteristics*

Calculations of the focal dose characteristics were performed assuming that the focus of the beams was positioned at the centre of a hemispherical phantom of tissue-equivalent material of 80 mm radius. A matrix of $50 \times 50 \times 50$ points was defined, which was aligned to the axis of the central source and extended $\pm 25.5$ mm from the focus in each of the three orthogonal directions. It was assumed that all sources were of equal activity and that the collimation of each gamma-ray beam was identical.

The measured transverse dose profile for the beam from a single source was used as the basis for calculating a point dose. The three beam profiles had been measured by the manufacturer using the appropriate geometry and a source–focus distance of 395 mm with the beam attenuated in 80 mm of water.

The dose contribution $D_i$ from the source i at a point A within the phantom (Fig. 11) is given by:

$$D_i = \left[\frac{f}{f-z}\right]^2 e^{\mu z}\, P(d)$$

where $f$ = the source–focus distance,

$z$ = the distance, projected along the beam axis, of the point A from the focus,

$\mu$ = linear attenuation coefficient for tissue for a photon energy of 1.25 MeV (the mean energy of the 1.17 MeV and 1.33 MeV photons emitted by cobalt 60), and

$P(d)$ = relative dose on the transverse dose profile at a distance $d$ from the beam axis.

The total dose at the point A is the sum of contributions from all 201 sources. The relative dose distribution is then normalised to the dose at the geometric focus.

The calculated dose distributions were verified experimentally. Figure 12 shows the phantom used. It consists of a hemisphere of Mix D (Jones & Raine, 1949) which was initially cast into a cylinder and machined to form a hemisphere. A Perspex base plate was attached and a protective shell of 1 mm-thick cabulite butyrate sheet was vacuum formed around the hemisphere. A cylindrical hole of 70 mm diameter was machined through the base into the hemisphere to a depth of 35 mm beyond the centre, to take a series of Perspex inserts which were designed to locate and support the ionisation chamber and silicon diodes.

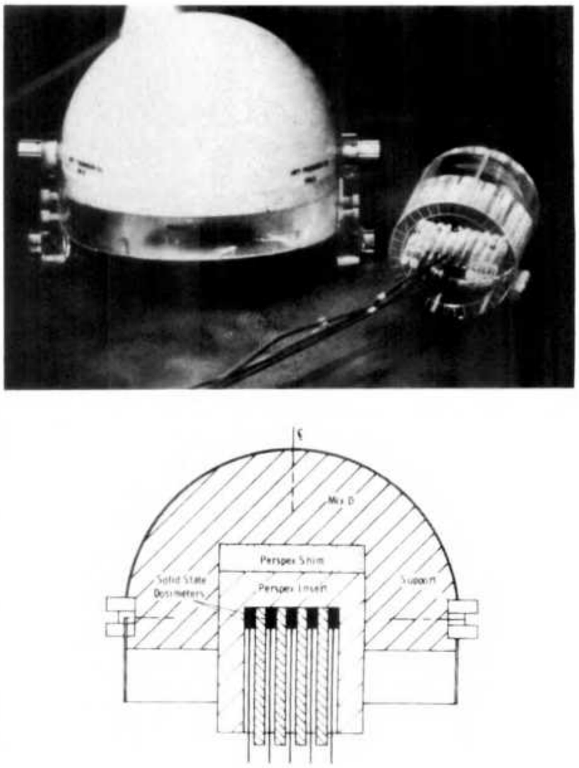

FIG. 12.
The hemispherical phantom used for calibration and verification of the focal dose characteristics.

The verification was carried out using the Therados DPD-5 radiotherapy dosemeter with five RFA-type detectors. These are silicon PN-junction diodes. The high sensitivity of the diode results in a small detector with good spatial resolution, which was essential in this application. The active element of the diodes is 2 mm × 2 mm × 0.05 mm, screened with a thin layer of aluminium, encapsulated in epoxy resin and sealed in a Perspex build-up cap of outer diameter 5 mm and length 10 mm.

The detectors were calibrated against an ionisation chamber at a known depth in a calibration block, irradiated by an 18 cm × 18 cm field from a conventional cobalt-60 radiotherapy unit.

The dosemeters were mounted in one of two cylindrical Perspex inserts. These have an array of holes along one diameter, with the centres of adjacent holes separated by the hole diameter. A detector could be positioned in any of the four holes. One insert has nine holes, one of which is along the central axis, whilst the second has 10 holes which are offset from the centre such that they provide measurement points between those of the first insert. These allowed measurements to be made, at intervals of 2.5 mm, up to 22.5 mm from the central plane of the phantom. The five detectors were placed in the holes and secured in position. Vacant holes were filled with Perspex plugs.

The exact location of the active element of the detectors with respect to the central planes of the phantom was determined radiographically. The precise distance from the centre of the insert to the centre of each active element was established. The phantom was supported in the helmet with the centre of the hemisphere positioned at the focus of the beams and with the central axis of the phantom aligned with the beam from the central source.

The dose distribution in one of the principal planes was determined by making sequential measurements, as the cylindrical insert and, therefore, the array of dosemeters was rotated in the phantom. Measurements were made at 20° intervals over 180°, with a 2 min exposure (approximately 5 Gy) at each interval. The detectors were then repositioned such that they occupied previously vacant positions and the procedure repeated. The order in which the probes were placed was varied to minimise the effect of errors in the calibration of individual probes. The dose distribution in the other two principal planes was established by first rotating the array of detectors to the angle of the plane required. Sequential sets of dose values were then measured, with the array at different depths within the phantom, by varying the thickness of the Perspex shim.

Figure 6 shows the measured and calculated distributions obtained in two of the principal planes of the 14 mm helmet. It can be seen that the computed results adequately represent the distribution of dose around the focus. A slightly poorer agreement between measured and calculated dose distributions for the 4 mm helmet was obtained. This is most probably a result of the small number of measurement points available and an inadequacy in the spatial resolution of the detectors, when operating in a dose gradient of 35% $\mathrm{mm}^{-1}$.

*Helmet relative output factors*

The calibration of the unit, in terms of dose rate at the focus, is based on the 14 mm helmet. The dose rate at the focus of the other helmets is related to the calibration by means of relative output factors. The measurements made to establish these were carried out using the Therados solid-state dosemeters.

One detector was positioned within the Perspex insert at the centre of the hemispherical phantom The phantom was positioned centrally within the helmet and the detector irradiated for 2 min. Three further measurements were then recorded, the insert being rotated by 90° between each measurement in order to minimise the effect of any errors in the centring of the probe. This procedure was carried out for each of the available five probes, providing a total of 20 dose measurements (approximately $5.0 \pm 0.04$ Gy) at the focus, which were averaged. The procedure was repeated for each of the three helmets.

The relative output factors for the three helmets are given in Table I.

*Calibration*

The calibration of the output dose rate of the unit was performed using a Farmer ionisation chamber (Nuclear Enterprises Type 2577), which had been previously calibrated against a National Physical Laboratory secondary standard. The thimble chamber, which has a sensitive volume of 0.22 $\mathrm{cm}^3$ (active length 8 7 mm × 6.3 mm diameter), was positioned in a Perspex insert at the centre of the calibration phantom and mounted at the focus of the 14 mm helmet. The centre of the sensitive element was thus positioned at the point of peak dose, with the extreme ends of the active volume within the 98% dose level. Four measurements of 4 min duration (approximately 10 Gy) were recorded, with the insert rotated by 90° between each reading. The average of the four readings was then appropriately corrected to yield the dose rate at the focus. The procedure was repeated five times to ensure reproducibility. The dose rate in September 1985 was 2.95 Gy $\mathrm{min}^{-1}$ at the focus of the 14 mm helmet.

The focal dose rate indicated by the ionisation chamber was noted to be about 12% higher than that

TABLE I

Helmet collimator relative output factors

| Helmet | Output factor |
|---|---|
| 14 mm | 1.0 |
| 8 mm | 0 964 |
| 4 mm | 0 925 |

obtained using the Therados probes. This discrepancy was found to result from the poor polar response of the probes.

## PATIENT INVESTIGATION AND TREATMENT

The treatment of a patient is reliant upon accurate localisation of the lesion and correspondingly accurate positioning of the patient for the subsequent treatment. The desired accuracy is achieved using a stereotactic frame which is secured to the patient by four 5 mm-diameter aluminium pins which penetrate the outer table of the skull to a depth of 3 mm. The frame has an orthogonal co-ordinate system engraved upon it which forms a base for the localisation, dose planning and single treatment. The three stages of the procedure are performed in sequence during a single session of 4–6 h. The frame is then removed.

### *Localisation*

A radiological examination is carried out with the frame attached to the patient, the type of investigation selected being the best one to identify the lesion, *e.g.* computed tomography (CT), angiography, etc.

In order to localise a lesion by means of a CT scan, two side plates are attached to the frame. These have three aluminium markers, two of which enable the magnification of the CT scan image to be measured. Two of the three co-ordinates for the lesion can then be determined directly from the film. This is achieved by measuring the distance in the appropriate plane between the markers and the lesion, correcting the value obtained for magnification and applying a correction to account for any offset in the origin of the co-ordinate system. The third marker is a 45° diagonal. The position of this marker on the CT image is dependent upon the level of the CT slice. The measurement of the distance between this marker and one of the fixed markers can be corrected to give the third co-ordinate of the lesion.

Figure 13 shows one slice of a CT scan of a patient with a pituitary stalk tumour, showing the stereotactic frame, side plates and markers.

In order to localise a lesion using conventional plain radiographic views, a co-ordinate cage is secured in position on the frame. This has a set of engraved scales, which align with the scales on the base and which are filled with wolfram (tungsten ore) so that they become visible on a lateral or antero-posterior radiograph of the patient. Figure 14 shows the lateral skull radiograph of a patient undergoing angiography for localisation of a cerebral arteriovenous malformation. The frame scales are visible and the three co-ordinates for the lesion can be calculated from readings taken from the images of the scales.

### *Dose planning*

The calculation of the three-dimensional dose distribution around a lesion is carried out on a Research Machines NIMBUS microcomputer. The computations take into account the position of the lesion within the skull, which is assumed to be ellipsoidal over the irradiated surface. The co-ordinates of the centre of the ellipsoid, together with the lengths of the half-axes, are determined from the radiographs. The dose due to all 201 sources is then calculated at 31 × 31 × 31 points arranged in a cube around the lesion. The calculations need to be performed while the patient waits, with the frame secured to the head, for treatment. Therefore, they need to be performed in a reasonable time and some approximations have to be made. The calculations are performed according to a technique initially proposed by Ahnesjo (1982) and further developed in Sheffield and take approximately 10 min for each focus.

Initial values are first interpolated from the standard pre-calculated distribution. The values obtained from

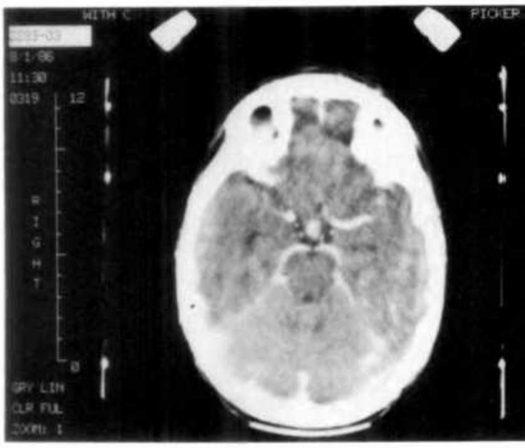

FIG. 13.

Computed tomogram for stereotactic localisation of a pituitary stalk tumour.

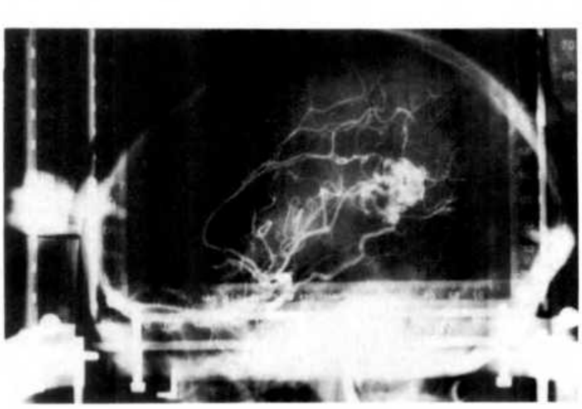

FIG. 14.

Angiogram for stereotactic localisation of an arteriovenous malformation.

this all assume that the focus is at the centre of a hemisphere and, therefore, they require that a correction be applied to take account of the actual skull shape. In order to determine the extent of the correction which must be applied, an exact dose value is calculated for every third point in the matrix. These values are the summation of the contributions from all sources at the point. The path length in tissue of each beam is calculated and the intensity of the beams corrected for the resultant attenuation. The ratio between the exact and the corresponding initial value for a point gives a measure of the attenuation correction required at the point in the distribution. Correction factors for the intermediate points in the initial distribution can then be interpolated from the factors obtained at every third point. The corrections are applied to the initial matrix of values.

A series of exact values is calculated for the points closest to the focus since the interpolation techniques produce the largest errors in this area where the dose gradients change most rapidly. The interpolation techniques produce a dose distribution for which the error in the dose is less than 1% of the maximum dose value for 97% of the points.

Adjacent foci can be superimposed with appropriate weighting factors to produce a larger or an unconventionally shaped distribution which is tailored to suit the lesion to be treated, *e.g.* a crescent shaped arteriovenous malformation within the choroidal fissure conforming to the shape of the trigone.

### *Treatment*

In order to treat the patient, two bearings are attached to the sides of the frame. These bearings are locked in position according to two of the pre-determined co-ordinates so that the lesion to be treated lies directly between them. The patient is then transferred to the couch of the treatment unit and the head positioned within the collimator helmet. This has two trunnions, precisely aligned with the focus, which engage the frame bearings. A lateral movement of the frame, patient's head and trunnions then serves to position the patient according to the third co-ordinate. The head is securely locked in position before treatment commences.

When the preparations are complete and the staff have left the treatment room, the couch and patient are moved into the treatment position. The irradiation of the patient and the treatment timer starts when the helmet finally aligns with the source-core collimation. A simple treatment delivering a peak dose of around 50 Gy is normally completed in approximately 20 min, after which the couch and patient are automatically withdrawn. The back-up timer measures the total transit plus treatment time, adding approximately 2 min to the set time. The radiographer can talk to the patient throughout and see the patient on the closed-circuit television systems. The treatment can be interrupted at any stage if required.

Where a more complex treatment plan has been prescribed, the co-ordinates can be reset before continuing with a second or subsequent irradiation using the same or a different helmet. All the irradiations must be completed in a single session before the stereotactic frame is removed from the patient and all the localisation reference data are lost.

### *Verification of localisation and treatment procedure*

In order to establish that the localisation and treatment procedures could be carried out accurately, a series of test irradiations was performed. A metal pin was used to pierce a hole in a therapy verification film and was pushed through until the pinhead touched the film. The film and pin were then sandwiched between two layers of a RANDO phantom head. The stereotactic frame was securely attached to the phantom and the pinhead localised radiographically. The co-ordinates of the pinhead were then used to position the phantom within the treatment unit and the phantom was irradiated. Figure 15 shows a film irradiated in this manner. The hole in the film can be seen to be centrally placed within the exposed area of film and confirms that no errors occurred in the localisation and treatment procedures.

### *Secondary dose to the patient*

Table II shows the secondary dose received by a patient undergoing a treatment of 20 min duration with the 14 mm helmet. The dose to the scalp was measured with the head in a central position. If a lesion is treated which is in a lateral position within the skull, the dose to an area on one side of the scalp increases to a level within the range 1.39–4.00 Gy. This occurs on the side closest to the focus, where the beam entry points are concentrated in a smaller area of scalp.

## Patient Safety

Wherever possible, the relevant British Standards were applied in the manufacture of the unit. In particular, the control panel of the unit was manufac-

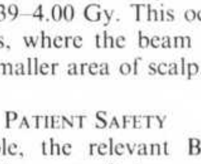

Fig. 15.

A verification radiograph, irradiated within a phantom head. The central hole marks the location of a pinhead, the stereotactic co-ordinates of which were used to position the phantom within the 14 mm helmet.

TABLE II

Secondary dose to patient for a 20 min treatment with 14 mm helmet *in situ*

| Location | Typical dose (Gy) |
|---|---|
| Prescribed peak target dose | 50.00 |
| Scalp (in region of beam entry) | 0.50 |
| Scalp (outside region of beam entry) | 0.10 |
| Thyroid | 0.13 |
| Sternum | 0.10 |
| Umbilicus | 0.07 |
| Small of back | 0.05 |
| Scrotum | 0.03 |
| Knees | 0.01 |

tured in accordance with the *Specification for the Safety of Medical Electrical Equipment* (British Standards Institution (BSI), 1979) whilst the dual-timer system was constructed in accordance with RASMP/75 (DHSS, 1975)

In the event of loss of electrical power, the couch automatically retracts from the treatment position and the shutter closes under reserve hydraulic pressure. The couch can be manually withdrawn from the treatment position should the reserve hydraulic pressure fail. A manually operated hydraulic pump can then be used to close the shutter Should either of these emergency withdrawal procedures fail, it would be possible to release the patient from the helmet trunnions using an extended key and the patient could then be removed from the couch.

## Clinical Evaluation

The commissioning of the unit was completed in early September 1985. The first patient, a 13-year-old girl with a cerebral arteriovenous malformation, was treated on September 18, 1985. Treatments have continued at the rate of one per week until June 1986 (31 patients treated) when the frequency was increased to two per week. The project has been financed on the basis that this frequency will be maintained throughout the 5-year evaluation period

The majority of lesions treated to date have been arteriovenous malformations. The time after treatment for their total obliteration is known to be at least 7 months (Steiner et al, 1977) and, therefore, follow-up angiography will not be performed until 12 months after treatment. Clinical results will be detailed in later reports.

## Acknowledgments

We would like to acknowledge the assistance given by our colleagues, Dr J. D. Bradshaw, Consultant Radiotherapist, and Mr D M C Forster, Consultant Neurosurgeon, who is the medical director of the unit Thanks are also extended to Miss J Boorman (Secretary) for her assistance in preparing the manuscript and to the Department of Medical Illustration, Royal Hallamshire Hospital, Sheffield

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# Average soft-tissue and bone models for use in radiation dosimetry

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(*Received November 1986*)

ABSTRACT

Average tissue compositions have been derived for seven groups of soft tissues found in "Reference Man". The analyses took into account some 40 soft tissues comprising the adult human. Different groups of soft tissues were selected to provide average tissue compositions of practical value in radiation dosimetry. In addition, as more reliable skeletal tissue data are now available, an updated tabulation is given of average bone formulations Elemental compositions and mass and electron densities are tabulated for all of the derived systems

A single elemental composition representing either a group of similar body tissues, such as soft tissues (International Commission on Radiation Units and Measurements (ICRU), 1969), or a discrete biological system made up of several similar components, such as bones (Woodard & White, 1982), has many applications in radiation dosimetry. For example, average tissue compositions are used in neutron dosimetry (ICRU, 1977), in the evaluation of dose equivalents in radiation protection (ICRU, 1980, 1985) and in the production of tissue substitutes for use in the manufacture of dosimetric phantoms for such techniques as mammography (White & Tucker, 1980).

In order to derive appropriate average tissue compositions, reliable elemental data must be available on the wide range of human body tissues, together with the proportions of these tissues in typical, or reference, subjects. The lack and unreliability of these data has, in the past, contributed to the computational problems. Unfortunately, the exact methods adopted in calculating the average compositions, including any weighting considerations, are often unclear in previous reported studies.

Following the recent reassessment of body tissue compositions (Woodard & White, 1986), it was realised that a comprehensive reappraisal of average soft tissue was feasible. Average tissue compositions for seven different groups of soft tissues were subsequently derived for the healthy adult male and female human. These were based on the new tissue compositions (extended to include six more biological systems) and modified versions of the body tissue proportions given by the International Commission on Radiological Protection (ICRP) (1975) for reference male and female.

The average elemental compositions of 24 bones (Woodard & White, 1982) have also been reappraised. This follows changes in the elemental compositions of the skeletal tissues, namely osseous tissue, red and yellow marrow, cartilage and spongiosa.

The results of these computations are presented in this paper. Elemental data and mass and electron densities are tabulated for all of the derived average tissue compositions.

## MATERIALS AND METHODS

### *Average soft tissues*

In this paper "soft tissues" are defined as body tissues remaining in a human subject (male or female) when osseous tissue, teeth, hair and nails are removed. Soft tissues comprise all the body fluids and those tissues radiologically similar to water and fat in the body.

Tissue proportions in the male and female human have been given in the "Reference Man" report published by ICRP (1975), although the data for the female are incomplete. Table I gives the masses of some 40 specific soft tissues making up a 70 kg male and a 58 kg female. The group called "miscellaneous soft tissues/body fluids" by ICRP, derived by difference to adjust the summated tissue masses to the required value, has been omitted. The masses quoted in Table I are based on the information provided by ICRP, corrected for inconsistencies in the male and female data and missing masses in those for the female. The tabulation also includes the water content of each tissue (Woodard & White, 1986), used later for characterisation when the soft-tissue groups are being selected for analysis.

The sum of the soft-tissue masses listed in Table I for the male is 62 658 g. The remaining tissue masses making up the whole body are osseous tissue (6260 g), teeth (46 g), hair (20 g), nails (3 g) and, by difference, miscellaneous soft tissues/body fluids (1013 g). For the female, the sum of the soft tissues is 52 590 g, with the remaining tissue masses being osseous tissue (5030 g), teeth (41 g), hair (150 g), nails (3 g) and, again by difference, miscellaneous soft tissue/body fluids (186 g).

Skeletal tissue masses for both male and female have been modified from those given by ICRP (1975) which depend, at least indirectly, on the work of Mechanik (1926). As most of Mechanik's seven male and six female cadavers were emaciated, with mean body masses of 61.9 kg and 49 9 kg respectively, the ratio of skeletal masses to body masses cannot be extrapolated to reference adult masses with any confidence. The 10 male and 10 female cadavers reported by Borisov and

Marei (1974) had mean body masses of 73.8 kg and 63.4 kg respectively and were close enough to the 70 kg and 58 kg for reference male and female to facilitate normalisation. The figures reported by Borisov and Marei are, however, for osseous tissue *plus* marrow, so the corresponding fraction of each tissue has to be obtained from Mechanik's data. Both Borisov and Marei *and* Mechanik removed cartilage and periarticular tissue before establishing the masses of the bones, which appears to have been overlooked in the Reference Man report. Consequently, the mean ratio of 0.142 for the masses of cleaned bones (male and female) compared with body mass was used to determine the mass of osseous tissue plus marrow (Borisov & Marei, 1974). The proportions accepted for osseous tissue to marrow were 63/37 (% by mass) for the male and 61/39 (% by mass) for the female (Woodard & Holodny, 1960; Bigler & Woodard, 1976). Marrow masses were attributed equally to red and yellow marrow.

The masses for the cartilage and periarticular tissue

TABLE I

THE SOFT BODY TISSUES IN REFERENCE ADULT MALE AND FEMALE

| Body tissue | Water content (%) ($P_w$) | Tissue mass (g) 70 kg male | Tissue mass (g) 58 kg female |
|---|---|---|---|
| Muscle—skeletal | 74.1 | 28 000 | 17 000 |
| Adipose tissue | 21.2 | 12 500 | 17 000 |
| Blood | 79.0 | 3690 | 3060* |
| Skin | 65.3 | 2600 | 1790 |
| Skeleton—red marrow | 39.7 | 1840 | 1605 |
| Skeleton—yellow marrow | 15.3 | 1840 | 1605 |
| Liver | 74.5 | 1800 | 1400 |
| Separable connective tissue | 60.4 | 1600 | 1300 |
| Central nervous system—brain | 75.6 | 1400 | 1200 |
| Gastrointestinal tract—intestine | 80.6 | 1200 | 1100 |
| Skeleton—cartilage | 75.0 | 1100 | 910 |
| Gastrointestinal tract—contents | 59.9 | 1005 | 835* |
| Lungs (two) | 79.8 | 1000 | 800 |
| Skeleton—periarticular tissue | 75.0 | 900 | 750 |
| Heart | 75.9 | 330 | 240 |
| Kidneys (two) | 76.6 | 310 | 275 |
| Lymph | 91.9 | 250 | 205* |
| Blood vessels | 72.1 | 200 | 165* |
| Spleen | 78.7 | 180 | 150 |
| Central nervous system—cerebrospinal fluid | 99.0 | 120 | 100 |
| Urinary bladder—urine | 96.3 | 102 | 102 |
| Aorta | 72.1 | 100 | 85* |
| Pancreas | 73.3 | 100 | 85 |
| Salivary glands (six) | 81.8 | 85 | 70 |
| Tongue | 74.1 | 70 | 60 |
| Gallbladder—bile | 88.4 | 62 | 50* |
| Urinary bladder—wall | 74.1 | 45 | 45 |
| Testes (two) | 82.7 | 35 | — |
| Central nervous system—spinal cord | 75.6 | 30 | 28 |
| Larynx | 74.1 | 28 | 19 |
| Thymus | 81.8 | 20 | 20 |
| Thyroid | 78.4 | 20 | 17 |
| Prostate | 83.3 | 16 | — |
| Ureters (two) | 74.1 | 16 | 15 |
| Eyes (two) | 87.4 | 15 | 15 |
| Adrenal glands (two) | 58.1 | 14 | 14 |
| Gallbladder | 74.1 | 10 | 8 |
| Trachea | 74.2 | 10 | 8 |
| Urethra | 74.1 | 10 | 3 |
| Miscellaneous glands | 81.8 | 5 | 5 |
| Breasts (two) | 31.3 | — | 360 |
| Uterus | 74.1 | — | 80 |
| Ovaries (two) | 82.8 | — | 11 |

*Data not present in Reference Man—ratio 58/70 of male values used.

were as quoted by ICRP (1975) for the male, while those for the female were derived from these values corrected for the difference in the body masses (×58/70). Similar corrections were used for the masses of female blood, gastrointestinal tract—contents, lymph, blood vessels, aorta and gallbladder—bile, which were not given by ICRP.

For the female, the mass of the hair is quoted as 300 g in the Reference Man report. As shorter hairstyles are now more popular, half this value was accepted.

The elemental compositions used for the majority of soft and skeletal tissues listed in Table I were as reviewed by Woodard and White (1986). The compositions of the body tissues not considered in this review, which make up 5.4% and 6.3% of the body masses for the male and female respectively, were established as follows

*Blood vessels.* The data for aorta were used, decreasing the calcium content by 0.1% and increasing the oxygen content by 0.1%

*Breasts.* A composition based on mammary gland (33.3) and adipose tissue (66.7) (% by mass) was adopted.

*Central nervous system—brain and spinal cord.* Both tissues were assumed to comprise grey matter (50) and white matter (50) (% by mass).

*Eyes.* Approximately 4 g of a 7.5 g eye is vitreous humour, which was assumed to be made up of water (99) and protein (1) (% by mass). The remaining 3.5 g (sclera, cornea, conjunctiva, iris, etc.) was given the composition of muscle—skeletal.

*Gastrointestinal tract—contents.* The composition was based on water (59.9), lipid (13), protein (13), carbohydrate (13) and mineral (1.1) (% by mass). The mineral content was based on that of muscle—skeletal, with the addition of 0.1% calcium

*Gastrointestinal tract—intestine.* In the absence of reliable data, the elemental compositions of the large and small intestine were taken as being identical and equivalent to that quoted by Woodard and White (1986) for the small intestine (wall).

*Miscellaneous glands (including salivary and thymus).* The average of the compositions of testis, ovary, thyroid and prostate was used.

*Tongue, larynx, ureters, urethra and uterus* These were all assumed to be the same as muscle—skeletal.

The elemental compositions of the six new formulations mentioned above are listed in Table II

For a given group of soft tissues, an average composition can readily be calculated from the elemental composition of each tissue and its proportion. by mass, in the group. The "average soft tissue" derived in this way is equivalent to a material representing a homogeneous mixture of the group of tissues. These calculations have been performed for the following groups of soft tissues, considering both male and female data.

Group 1. All soft tissues listed in Table I
Group 2. As Group 1, omitting adipose tissue and yellow marrow
Group 3. As Group 1, omitting red and yellow marrow, cartilage and periarticular tissue
Group 4. $80 < P_w \leqslant 100$ where $P_w$ = water content (% by mass)
Group 5. $60 < P_w \leqslant 80$
Group 6. $40 < P_w \leqslant 60$
Group 7. $20 < P_w \leqslant 40$

By removing the major fatty tissues, Group 2 represented the water-like tissues, while Group 3 represented the soft tissues remaining when those associated with skeleton are removed. Groups 4–7 contained soft tissues with water contents within specified narrow intervals.

### Average bones

Woodard and White (1982) evaluated the proportions, by mass, of the skeletal tissues making up the

TABLE II

ELEMENTAL COMPOSITIONS OF THE BODY TISSUES NOT CONSIDERED BY WOODARD AND WHITE (1986)

| Body tissue | Elemental composition (% by mass) | | | | | Densities | | |
|---|---|---|---|---|---|---|---|---|
| | H | C | N | O | Elements with $Z > 8$ | Mass kg $m^{-3}$ | Electron | |
| | | | | | | | electrons $kg^{-1} \times 10^{26}$ | electrons $m^{-3} \times 10^{26}$ |
| Blood vessels | 9.9 | 14.7 | 4.2 | 69.9 | Na(0.2); P(0.4), S(0.3); K(0.1); Ca(0.3) | 1050 | 3.303 | 3468 |
| Breasts | 11.1 | 51.0 | 1.5 | 36.1 | Na(0.1), S(0.1); Cl(0.1) | 970 | 3.338 | 3238 |
| Central nervous system—brain<br>Central nervous system—spinal cord | 10.7 | 14.5 | 2.2 | 71.2 | Na(0.2); P(0.4), S(0.2), Cl(0.3), K(0.3) | 1040 | 3.327 | 3460 |
| Eyes | 10.7 | 6.9 | 1.7 | 80.3 | P(0.1), S(0.1); K(0.2) | 1020 | 3.328 | 3395 |
| Gastrointestinal tract—contents | 10.0 | 22.2 | 2.2 | 64.4 | Na(0.1); P(0.2); S(0.3), Cl(0.1), K(0.4); Ca(0.1) | 1030 | 3.306 | 3405 |
| Miscellaneous glands | 10.5 | 10.0 | 2.3 | 76.3 | Na(0.2); P(0.1); S(0.2), Cl(0.2), K(0.2) | 1050 | 3.321 | 3487 |

bones in 23 body sites. The evaluation covered the principal bones, including the cranium and mandible, vertebrae, ribs, pelvic bones, humerus and femur. Following the recent reassessment of, and changes in, the compositions of skeletal tissues (osseous tissue, red and yellow marrow, cartilage and spongiosa) the elemental compositions of the average bone formulations presented in this earlier paper have been recalculated. An additional formulation for femur (total bone) is included.

Mass and electron densities were calculated for both average soft tissues and average bone formulations. Mass and volume electron densities (electrons per kg and electrons per m$^3$) were calculated from the elemental atomic weights, Avogadro's number ($6.022045 \times 10^{26}$ kmol$^{-1}$) (Handbook of Chemistry and Physics, 1984) and the computed mass densities.

## Results

The elemental compositions for the average tissue formulations quoted in this section include all the elements present with proportions $\geqslant 0.1\%$ by mass. Minor rounding errors were generally no more than 0.1%, by mass, and were attributed to the major element present, namely oxygen. Mass densities are corrected to three significant figures, electron densities are quoted to four significant figures

### *Average soft tissues*

The compositions of the average soft tissues are listed in Table III. Elemental compositions (% by mass) and mass and electron densities are given for the seven groups of soft tissues considered. Data for the male and female are included. The number of body tissues present in each group is given in the first column of the table.

### *Average bones*

A summary of the proportions (% by mass) of the skeletal tissues in healthy, adult human bones presented by Woodard and White (1982) is given in Table IV.

Table V lists the resulting elemental compositions (% by mass) and mass and electron densities when the recent elemental compositions of skeletal tissues (Woodard & White, 1986) are used in conjunction with the proportions in Table IV Data for the 24 average bone formulations are provided.

## Discussion

The calculation of average soft tissue presented here was based firmly on the data on Reference Man provided by ICRP (1975). The ICRP recognised that it is not feasible to define an average or median individual within a specified population, but agreed "... to select data primarily to represent what is believed might be a

TABLE III

Elemental compositions of the groups of average soft tissues

| Tissue group (M = male; F = female) | | Elemental composition (%, by mass) | | | | | Densities | | |
|---|---|---|---|---|---|---|---|---|---|
| | | H | C | N | O | Elements with $Z > 8$ | Mass kg m$^{-3}$ | Electron | |
| | | | | | | | | electrons kg$^{-1}$ × 10$^{26}$ | electrons m$^{-3}$ × 10$^{26}$ |
| Group 1 | M(40)* | 10.5 | 25.6 | 2.7 | 60.2 | Na(0.1), P(0.2), S(0.3), Cl(0.2); K(0.2) | 1030 | 3.320 | 3420 |
| (all soft tissues) | F(41) | 10.6 | 31.5 | 2.4 | 54.7 | Na(0.1); P(0.2); S(0.2), Cl(0.1), K(0.2) | 1020 | 3.324 | 3390 |
| Group 2 | M(38) | 10.2 | 15.3 | 3.3 | 70.0 | Na(0.1), P(0.3), S(0.3); Cl(0.2); K(0.3) | 1060 | 3.312 | 3511 |
| as Group 1 *except* adipose and yellow marrow) | F(39) | 10.2 | 15.8 | 3.3 | 69.4 | Na(0.2); P(0.3); S(0.3); Cl(0.2); K(0.3) | 1050 | 3.312 | 3478 |
| Group 3 | M(36) | 10.5 | 24.4 | 2.8 | 61.5 | Na(0.1); P(0.1), S(0.2); Cl(0.1), K(0.3) | 1030 | 3.320 | 3420 |
| (as group 1 *except* red and yellow marrow, cartilage and periarticular tissue) | F(37) | 10.6 | 30.8 | 2.4 | 55.5 | Na(0.1), P(0.1), S(0.2); Cl(0.1); K(0.2) | 1010 | 3.325 | 3358 |
| Group 4<br>$80 < P_w \leqslant 100$ | M(11)<br>F(10) | 10.7 | 8.9 | 1.8 | 77.8 | Na(0.2), P(0.1); S(0.1); Cl(0.3), K(0.1) | 1030 | 3.327 | 3427 |
| Group 5<br>$60 < P_w \leqslant 80$ | M(24)<br>F(25) | 10.2 | 14.3 | 3.4 | 70.8 | Na(0.2); P(0.3); S(0.3); Cl(0.2); K(0.3) | 1060 | 3.311 | 3510 |
| Group 6<br>$40 < P_w \leqslant 60$ | M(2)<br>F(2) | 10.0 | 22.3 | 2.2 | 64.3 | Na(0.1); P(0.2), S(0.3); Cl(0.1); K(0.4), Ca(0.1) | 1030 | 3.306 | 3405 |
| Group 7 | M(2) | 11.3 | 57.5 | 1.0 | 29.9 | Na(0.1); S(0.1); Cl(0.1) | 960 | 3.344 | 3210 |
| $20 < P_w \leqslant 40$ | F(3) | 11.3 | 58.2 | 0.9 | 29.3 | Na(0.1); S(0.1); Cl(0.1) | 957 | 3.345 | 3201 |

*Number of soft body tissues in each group is given in parentheses.

typical individual of the European or American populations" (ICRP, 1975, p. 3). In addition, "Reference Man is defined as being between 20 and 30 years of age, weighing 70 kg, is 170 cm in height, and lives in a climate with an average temperature of from 10 to 20°C. He is a caucasian . . ." (ICRP, 1975, p. 4). The tissue proportions documented by ICRP, together with the few amendments and additions mentioned earlier, were accepted as being the most reliable set of data available on the relative distribution of body tissues in the adult male and female human.

It seemed prudent to omit the masses attributed to "miscellaneous soft tissues/body fluids" from the complete set of soft tissues considered (Table I). Such a category is derived (by difference) to account for any shortfall in the summated body tissue masses when compared with total body mass and by nature is of uncertain composition. Allocating the composition of muscle—skeletal or a mixture of equal parts muscle—skeletal and plasma, by mass, produced individual deviations in the elements H, C, N and O generally below 0.2%.

The seven groups of soft tissues were chosen so that the most appropriate grouping could be readily selected for a given dosimetric investigation. For many applications in radiation protection, one of the Groups 1–3 may be adequate, with the option of choosing a broad average (Group 1), an average of the water-like soft tissues (Group 2), or an average of the soft tissues not associated with the skeleton (Group 3). More elaborate radiation dosimetry may need the compositions from Groups 4–7, where soft tissues having water contents within defined narrow intervals are assessed. The use of any of these average compositions may simplify both theoretical dosimetry using organ or tissue models and the production of tissue substitutes for use in practical dosimetry, while still maintaining the requisite precision.

The relative masses of muscle—skeletal and adipose tissue are substantially different in the male and female.

TABLE IV

BODY TISSUE PROPORTIONS IN HEALTHY, ADULT HUMAN BONES (WOODARD & WHITE, 1982)

| Bone | Tissue proportions (% by mass) | | |
|---|---|---|---|
| | Osseous tissue | Red marrow | Other |
| Head (male and female) | | | |
| Cranium | 78.1 | 21.9 | |
| Mandible | 83.1 | 16.9 | |
| Male vertebral column | | | |
| Excluding cartilage | | | |
| C4 | 59.2 | 40.8 | |
| D6, L3 | 49.2 | 50.8 | |
| Including cartilage | | | |
| C4 | 52.9 | 36.4 | cartilage (10.7) |
| D6, L3 | 43.6 | 45.0 | cartilage (11.4) |
| Whole column | 46.7 | 42.2 | cartilage (11.1) |
| Male shoulder girdle | | | |
| Sternum | 37.8 | 62.2 | |
| Clavicle, scapula | 67.6 | | yellow marrow (32.4) |
| Male ribs | | | |
| 2nd, 6th | 58.3 | 41.7 | |
| 10th | 69.2 | 30.8 | |
| Humerus (total bone) | 67.5 | | yellow marrow (32.5) |
| Humerus (proximal 10 cm) | | | |
| Spherical head | 54.3 | | yellow marrow (45.7) |
| Cylindrical shaft | 70.1 | | yellow marrow (29.9) |
| Whole specimen | 59.8 | | yellow marrow (40.2) |
| Pelvic bones | | | |
| Innominate male | 58.5 | 41.5 | |
| female | 63.4 | 36.6 | |
| Sacrum male | 43.4 | 56.6 | |
| female | 55.4 | 44.6 | |
| Femur (total bone) | 63.7 | | yellow marrow (36.3) |
| Femur (proximal 17 cm) | | | |
| Spherical head | 54.3 | | yellow marrow (45.7) |
| Conical trochanter | 57.1 | | yellow marrow (42.9) |
| Cylindrical shaft | 89.9 | | yellow marrow (10.1) |
| Whole specimen | 64.2 | | yellow marrow (35.8) |

In the male, 44.7% of the total soft-tissue mass is muscle—skeletal and 19.9% is adipose tissue. These figures are both 32.3% in the female. The differences are evident in the results, with the two sets of compositions being similar when adipose tissue is not considered (Group 2). Adipose tissue is not included in the specialised Groups 4–6 and individual elements present are within 0.1% of each other, so a single composition for male and female is acceptable. The divergence reappears in Group 7, which includes adipose and other fatty tissues The categorisation used in Groups 4–7 covers all the tissues listed in Table I, except for yellow marrow, which is the only soft tissue with a water content below 20% (15.3%) by mass.

An elemental composition for *total soft tissue* was quoted by ICRP (1975). The derived H, C, N and O

TABLE V

ELEMENTAL COMPOSITIONS OF THE AVERAGE BONE FORMULATIONS

| Bone | Elemental composition (% by mass) | | | | | Densities | | |
|---|---|---|---|---|---|---|---|---|
| | H | C | N | O | Elements with $Z > 8$ | Mass kg $m^{-3}$ | Electron | |
| | | | | | | | electrons $kg^{-1} \times 10^{26}$ | electrons $m^{-3} \times 10^{26}$ |
| Head (male and female) | | | | | | | | |
| Cranium | 5.0 | 21.2 | 4.0 | 43.5 | Na(0.1), Mg(0.2); P(8.1); S(0.3), Ca(17.6) | 1610 | 3.148 | 5068 |
| Mandible | 4.6 | 19.9 | 4.1 | 43.5 | Na(0.1), Mg(0.2); P(8.6); S(0.3); Ca(18.7) | 1680 | 3.137 | 5270 |
| Male vertebral column | | | | | | | | |
| Excluding cartilage | | | | | | | | |
| C4 | 6.3 | 26.1 | 3.9 | 43.6 | Na(0.1), Mg(0.1); P(6.1); S(0.3); Cl(0.1); K(0.1), Ca(13.3) | 1420 | 3.190 | 4530 |
| D6, L3 | 7.0 | 28.7 | 3.8 | 43.7 | Mg(0.1); P(5.1), S(0.2); Cl(0.1); K(0.1), Ca(11.1), Fe(0.1) | 1330 | 3.212 | 4272 |
| Including cartilage | | | | | | | | |
| C4 | 6.6 | 24.3 | 3.7 | 47.1 | Na(0.1), Mg(0.1); P(5.7), S(0.3), Cl(0.1), K(0.1); Ca(11.9) | 1380 | 3.201 | 4417 |
| D6, L3 | 7.3 | 26.5 | 3.6 | 47.3 | Na(0.1); Mg(0.1), P(4.8); S(0.3); Cl(0.1), K(0.1), Ca(9.8) | 1300 | 3.221 | 4187 |
| Whole column | 7.1 | 25.8 | 3.6 | 47.2 | Na(0.1); Mg(0.1); P(5.1); S(0.3); Cl(0.1); K(0.1); Ca(10.5) | 1330 | 3.214 | 4275 |
| Male shoulder girdle | | | | | | | | |
| Sternum | 7.8 | 31.6 | 3.7 | 43.8 | Mg(0.1); P(4.0); S(0.2); Cl(0.1); K(0.1); Ca(8.5), Fe(0.1) | 1250 | 3.237 | 4046 |
| Clavicle, scapula | 6.0 | 31.3 | 3.1 | 37.0 | Na(0.1); Mg(0.1), P(7.0), S(0.2), Ca(15.2) | 1460 | 3.181 | 4644 |
| Male ribs | | | | | | | | |
| 2nd, 6th | 6.4 | 26.3 | 3.9 | 43.6 | Na(0.1), Mg(0.1); P(6.0); S(0.3), Cl(0.1), K(0.1); Ca(13.1) | 1410 | 3.192 | 4501 |
| 10th | 5.6 | 23.5 | 4.0 | 43.4 | Na(0.1), Mg(0.1), P(7.2); S(0.3); Cl(0.1), K(0.1); Ca(15.6) | 1520 | 3.168 | 4815 |
| Humerus (total bone) | 6.0 | 31.4 | 3.1 | 36.9 | Na(0.1), Mg(0.1), P(7.0); S(0.2), Ca(15.2) | 1460 | 3.181 | 4644 |
| Humerus (proximal 10 cm) | | | | | | | | |
| Spherical head | 7.1 | 37.9 | 2.6 | 34.2 | Na(0.1); Mg(0.1), P(5.6); S(0.2); Ca(12.2) | 1330 | 3.214 | 4291 |
| Cylindrical shaft | 5.8 | 30.1 | 3.2 | 37.4 | Na(0.1); Mg(0.2); P(7.2); S(0.2); Ca(15.8) | 1490 | 3.175 | 4737 |
| Whole specimen | 6.7 | 35.2 | 2.8 | 35.2 | Na(0.1), Mg(0.1), P(6.2), S(0.2), Ca(13.5) | 1390 | 3.200 | 4435 |
| Pelvic bones | | | | | | | | |
| Innominate male | 6.3 | 26.2 | 3.9 | 43.6 | Na(0.1); Mg(0.1); P(6.1); S(0.3); Cl(0.1); K(0.1); Ca(13.2) | 1410 | 3.191 | 4499 |
| female | 6.0 | 25.0 | 3.9 | 43.5 | Na(0.1), Mg(0.1), P(6.6), S(0.3), Cl(0.1), K(0.1), Ca(14.3) | 1460 | 3.181 | 4644 |
| Sacrum male | 7.4 | 30.2 | 3.7 | 43.8 | Mg(0.1); P(4.5); S(0.2); Cl(0.1); K(0.1); Ca(9.8); Fe(0.1) | 1290 | 3.225 | 4160 |
| female | 6.6 | 27.1 | 3.8 | 43.5 | Na(0.1), Mg(0.1), P(5.8), S(0.3), Cl(0.1), K(0.1); Ca(12.5) | 1390 | 3.198 | 4445 |
| Femur (total bone) | 6.3 | 33.3 | 2.9 | 36.2 | Na(0.1); Mg(0.1), P(6.6); S(0.2); Ca(14.3) | 1420 | 3.191 | 4544 |
| Femur (proximal 17 cm) | | | | | | | | |
| Sperical head | 7.1 | 37.9 | 2.6 | 34.2 | Na(0.1), Mg(0.1); P(5.6); S(0.2); Ca(12.2) | 1330 | 3.214 | 4291 |
| Conical trochanter | 6.9 | 36.6 | 2.7 | 34.7 | Na(0.1); Mg(0.1), P(5.9); S(0.2); Ca(12.8) | 1360 | 3.207 | 4363 |
| Cylindrical shaft | 4.2 | 20.4 | 3.8 | 41.5 | Na(0.1); Mg(0.2); P(9.3); S(0.3); Ca(20.2) | 1750 | 3.125 | 5471 |
| Whole specimen | 6.3 | 33.1 | 2.9 | 36.3 | Na(0.1), Mg(0.1), P(6.6); S(0.2), Ca(14.4) | 1430 | 3.189 | 4558 |

contents are close to the Group 3 results for the male given in Table III.

The homogeneous phantom suggested by ICRU (1980, 1985) for applications in radiation protection is made up of a material representing an average soft-tissue composition of H(10.1), C(11 1), N(2.6) and O(76.2) (% by mass). Although this is not exactly matched by any of the compositions in Table III, it is perhaps closest to Group 5, the large set of soft tissues with water content between 60% and 80% by mass. It is interesting to note that an earlier "tissue approximation" introduced by ICRU (1969) and based on the formula $(C_5 H_{40} N O_{18})_n$ suggested by Rossi and Failla (1956) has the elemental composition H(10.0), C(14.9), N(3.5) and O(71.6) (% by mass), which is very close to the Group 5 composition.

Significant differences are evident in the elemental compositions of the average bone formulations compared with the data given earlier by Woodard and White (1982). In particular, the changes in spongiosa have affected the results for humerus (proximal 10 cm) and the femur (proximal 17 cm). Dependent upon the proportion of osseous tissue and yellow marrow, carbon contents differ by 16–52% and oxygen by 8–38% for these bones. For the remaining average bones, carbon is within 5% and oxygen is within 2% of the earlier data. The results for the higher-$Z$ element, calcium, are within 2% of previously reported values. Differences in mass densities are generally less than 1%, the result of the mass density of osseous tissue being changed from 1900 kg $m^{-3}$ to 1920 kg $m^{-3}$.

Further investigations are needed to establish similar average tissue compositions for paediatric subjects and to extend the work to other ethnic groups.

ACKNOWLEDGMENTS

The ICRU and the Joint Research Board of St Bartholomew's Hospital are thanked for funding part of this work

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# Book reviews

*Fourth International Radiopharmaceutical Dosimetry Symposium Proceedings.* Ed. by A T Schlafke-Stelson and E E Watson, pp x+737, 1986 (National Technical Information Service, US Dept of Commerce, Springfield), $48 00 (Also available on microfiche )
CONF 851113-(DE86010102)

This symposium was the fourth on radiopharmaceutical dosimetry, the previous one being held in 1980 The purpose was to present current internal dosimetry information on estimate methodology and research developments and needs. The proceedings contain 52 papers, including bibliographies submitted by the authors at a conference held at Oak Ridge, Tennessee on November 5–8, 1985. The quality of manuscript reproduction, including graphs and tables, is very good Image reproduction is satisfactory and does not hinder the conveyance of information by the authors

The major categories of the presented papers are microdosimetry, monoclonal antibodies, modelling and dose estimates, positron emitters, biokinetics, and the haemopoietic system. A few papers discuss the sociopolitical relevance of dosimetry benefits versus risks, US Food and Drug Administration requirements for radiopharmaceutical approval, and probability of causation of cancer.

Recent developments in microdosimetry (or cellular dosimetry as some prefer) methodology, particularly in providing estimates for monoclonal antibodies, are of major significance, and several papers give insight into and understanding of the concerns and problems associated with this dosimetry. These would be of particular interest to those applying monoclonal antibodies therapeutically.

On the macroscopic scale, the greatest portion of the presentations deals with the quantitative estimates and kinetics of non-positron emitters. The topics covered include several iodinated pharmaceuticals, effects of radiocontaminants and patient pathology, drugs altering biodistribution, conceptus and paediatric dose estimates, including breast feeding, labelled blood cell products, and models for blood, bone marrow, bladder wall, and thyroid.

Nine papers illustrate the considerations and concerns regarding dose estimates for positron and ultrashort-lived emitters Notable issues involve quantifying the administered activity and high dose rates at the administration site

The editors are to be highly commended for again providing noteworthy features seldom found in published proceedings The first is appending each paper with the participants' questions and author's responses This discussion is often interesting and enlightening. Also included is a symposium summary panel discussion that presented current concerns and needs for future internal dosimetry research Another feature is providing indexes for both subjects and authors A minor distraction was the inefficient use of entire pages for a single table or graph

This massive volume contains an array of valuable information at a very reasonable price. These proceedings are highly recommended to individuals interested in the dosimetry of nuclear medicine pharmaceuticals, especially for a better understanding of the issues concerning microdosimetry.

R P LIETO

*A Glossary of Physics, Radiation Protection and Dosimetry in Diagnostic Organ Imaging.* By B. D P. Williamson, J C Le Heron, J L. Poletti and P H. Cartwright, pp 172, 1985 (The World Radiography Educational Trust Fund, Cardiff), £6.75.

This glossary is intended by the authors to provide a ready reference for radiography students, radiology registrars and others studying radiation physics, protection and equipment in diagnostic radiology At a basic level it covers atomic physics and radioactivity, the production of X rays and interactions of radiation with matter, the main characteristics of X-ray equipment, radiation protection and dosimetry, relevant computer terminology and various aspects of the diagnostic imaging process, including the diagnostic uses of ultrasound, radionuclides and nuclear magnetic resonance

There is no doubt that the glossary is extremely comprehensive since there appears to be no major subject omitted from the contents Furthermore, the description and definition of the terms listed in the glossary are generally acceptable to all but the highly pedantic In only a few instances do the definitions include terminology which might not be easily understood by a new student to the subject (*e.g.* "FWHM" on page 25, "linear shift invariant system" on page 30, "FID" on page 152) and in one or two definitions the obvious need for brevity has resulted in phraseology which is not easily understood

The presentation would be better if figures and diagrams were numbered and referred to by number in the text. It is not always obvious which diagram is being referred to and in one instance ("Photometry" on page 117) the figure would appear to be absent from the text altogether.

Errors are few and in one instance ("x $cD^2$" instead of "$+cD^2$" on page 93) may simply be a printing error However, not everyone might agree with the statement on page 29 that systems that work well at low contrast will necessarily resolve smaller holes at low contrast, or on page 117 that the probability of photoelectric absorption interactions are inversely proportional to photon energy to the "fifth" power.

Despite these minor criticisms, however, the authors are to be complimented for their valiant efforts to fill a gap in publications of this type in this particular field. There is no doubt that, as intended, the glossary will greatly assist those preparing for examinations in medical radiation and X-ray physics and it is to these students that this publication can be recommended with confidence.

E T. HENSHAW

1987, *The British Journal of Radiology*, *60*, 915–918

SEPTEMBER 1987

# Radiation safety in the nuclear medicine department: impact of the UK *Ionising Radiations Regulations*

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(*Received January 1987 and in revised form March 1987*)

ABSTRACT

The practice of nuclear medicine requires integration of radiation safety with patient care and radiopharmaceutical standards Nationally there was useful discussion in the UK before the *Ionising Radiations Regulations* and *Approved Code of Practice* were published, although such consultation had been lacking when the Medicines Act was implemented. Most of the new considerations relating to nuclear medicine stem from Schedule 6 of the *Regulations*. Generally, the presence of a single patient does not require a controlled area. However, when several patients are present, or radiopharmaceuticals are being prepared prior to injection, a controlled area is required. Classification of workers is not likely to be required in a typical nuclear medicine department in the UK, although most parts of the nuclear medicine department will need to be controlled areas. These include the radiopharmacy, radionuclide dispensary, injection room, and imaging rooms if patients are injected in them. The importance of finger dose measurements is emphasised. Patient wards, however, need not be controlled areas. A particular concern in nuclear medicine was that patients should not need to be admitted to hospital merely to comply with legislation. This is possibly the case and clarification will probably be available when the *Notes for Guidance* are published. Most procedures in nuclear medicine departments will remain unchanged Further information is required, however, on patient waiting rooms, handling flood sources, pregnancy, and breast feeding. Within the hospital, detailed and multidisciplinary discussion will need to take place within the forum of the radiation safety committee.

Radiation safety should be everyone's concern; it is particularly important for the staff in a nuclear medicine department, but considerations must also include staff visiting the department, and patients and their friends or relatives. However, the practice of nuclear medicine requires integration of radiation safety with patient care, and radiopharmaceutical standards. Patient care implies not only their medical care, but that they should be dealt with as people, and not be subjected to unnecessary procedures which cause them stress. When the UK *Ionising Radiation Regulations* (*IRR*, 1985) and *Approved Code of Practice* (Health & Safety Commission, 1985) were in their draft forms, we were fortunately able to discuss their contents with representatives from the Health and Safety Executive and thereby avoid irksome restrictions. In contrast, the implications of the radiopharmaceutical standards required by the Medicines Act were not so carefully thought out, and as a result there were, and still are, inconsistencies and problems in their implementation.

In order to consider the implications of the *IRR*, *Code of Practice*, and as yet unconfirmed *Notes for Guidance*, it is necessary to define the average nuclear medicine department. The data of Wall et al (1985) show that such a department in the UK would undertake approximately 1600 nuclear medicine studies a year. Harding et al (1985a) have provided data which indicate that in a month the amount of activity handled for this number of studies is approximately 40 GBq of $^{99}Tc^{m}$, together with a number of other nuclides in much smaller quantities. While this appears to be a large amount of radioactivity, technetium is regarded as a relatively safe radionuclide; the 140 keV gamma emission is easily shielded and, because of its short half-life, long-term contamination is unlikely.

The most important section of the *IRR* with regard to nuclear medicine is Schedule 6. This defines controlled areas, basically as areas in which the instantaneous dose rate (measured over 1 min) exceeds 7.5 μSv per h. Inspectors will therefore be able to decide quickly whether an area needs to be "controlled" However, there are two important exemptions. If the activity is in a patient (or corpse) and the activity–energy product does not exceed 150 MBq MeV, or if the activity is in a syringe or bottle and the product does not exceed 50 MBq MeV, then the area need not be controlled (Table I). The activity–energy product is defined in terms of the activity and the total gamma energy per disintegration, which takes into

TABLE I

DEFINITION OF CONTROLLED AREAS

A Instantaneous dose rate 7.5 μSv per h (over 1 min).

B Exemptions

| | MBq MeV | MBq $^{99}Tc^{m}$ | MBq $^{131}I$ |
|---|---|---|---|
| Patients | 150 | 1215 | 429 |
| Syringe | 50 | 405 | 143 |

C Classification
Body 1.2 mSv per month
Finger 12 0 mSv per month

Supervised area is required if one-third of any of these figures is exceeded

TABLE II

INTERNAL DOSE ASSESSMENT

| | $^{99}Tc^m$ | $^{131}I$ |
|---|---|---|
| Airborne (Bq per m$^3$) | $2.0 \times 10^5$ | $7.0 \times 10^1$ |
| Surface (Bq per cm$^2$) | $1.3 \times 10^5$ | $3.0 \times 10^1$ |

These figures are a third of those in *IRR* Schedule 2, where the conditions of their measurement are described

account the decay scheme of the radionuclide (0.1235 MeV for $^{99}Tc^m$, 0.35 MeV for $^{131}I$). As examples, 150 MBq MeV corresponds to 1215 MBq of $^{99}Tc^m$ or 429 MBq of $^{131}I$. These exemptions encompass all the routine doses authorised in *Administration of Radioactive Substances to Persons* (DHSS, 1984) (*ARSAC*) However, there are the overriding requirements that should the dose to the body exceed 1.2 mSv per month, or the dose to the fingers exceeded 12 mSv per month, then the person must be "classified" and the area must be "controlled". These figures are derived as 3/10 of the annual limits of 50 mSv for the body and 500 mSv for the fingers. A supervised area is required if a third of any of the above figures is exceeded.

Classification of workers is unlikely to be required in most nuclear medicine departments, and regular medical examinations are not therefore required. Those allowed to enter controlled areas are patients undergoing investigation or treatment, classified workers, and persons entering under a "written system of work" How this latter group conduct themselves within the controlled area so that they do not exceed the monthly limits (described in Table I, C) must be described in the system of work and incorporated into the local rules. Those working in nuclear medicine should continue to wear film badges and, on occasions, finger thermoluminescent dosemeters to ensure that they do not exceed the same dose limits If they are exposed to surface or airborne contamination likely to exceed one third of the figures in Schedule 2, examples of which are given in Table II, then they may need assessment of internal body dose, for example by monitoring thyroid uptake or whole-body counting Such levels are not likely to be exceeded in the case of $^{99}Tc^m$ but may well be in the case of $^{131}I$.

Detailed references to sections of the *IRR* and *Code of Practice* can be found in Harding et al (1986a). Radiation doses quoted in the remainder of this paper are derived from work (Harding et al, 1985a, b) undertaken specifically to assess the implications of the *IRR* to a nuclear medicine department, and relate to handling 40 GBq of $^{99}Tc^m$ per month.

## RADIOPHARMACY

The instantaneous dose rate over the radioactive bolus in a syringe is very large, of the order of 1000 mSv per h. This is clearly in excess of the instantaneous figure in Table I, A, but the whole-body doses from film-badge monitoring show that a monthly dose of less than 0.3 mSv is anticipated even in a fairly large radiopharmacy. Using tongs for remote handling of bottles and syringes wherever possible, the dose rate to the finger pulp is 4.8 mSv per 40 GBq $^{99}Tc^m$ if syringe shields are not used and 2.8 mSv if they are. The benefit derived from syringe shields could be particularly important in a large radiopharmacy, but they are necessary in any case to keep the dose rate as low as reasonably achievable (ALARA). A controlled area is required in the radiopharmacy because of the amount of activity in syringes.

## RADIONUCLIDE DISPENSARY

Some departments have a radionuclide dispensary where multidose vials are dispensed into individual syringes for patient doses. The 50 MBq MeV limit (Table I, B) is exceeded, but whole-body doses are less than 0.3 mSv per month. Typical doses to the finger pulp are 9.2 mSv without syringe shields and 7.2 mSv with syringe shields. The very small benefit of syringe shields is, of course, due to the fact that during a dose measurement no shields can be used, and taking the syringe shield on and off the syringe exposes the worker. Overall, however, there is benefit in using syringe shields and, if they are fitted in the radionuclide dispensary, there is a very useful reduction in finger dose rate at the time of injection. A controlled area is required in the radionuclide dispensary.

## INJECTION AREA

In the injection area the radioactive syringe again requires a controlled area, but the whole-body limit given in Table I, C, is not exceeded However, finger pulp doses at the time of injection can be quite large, and our measurements indicate a figure of 12 mSv for 40 GBq handled without syringe shields and 3 mSv with syringe shields. Not only is there clear benefit from syringe shields but the figure without shields is at the limit of classification, and workers would be required to be classified if a single person injected this amount of activity in a month without using syringe shields.

In the injection area great care is taken to identify the patient, find a vein, and to clean the skin *before* the lead box containing the syringe is opened. Immediately after injection the syringe is returned to the lead box. The fact that the patient now contains all the activity which

TABLE III

TOTAL DOSE ($\mu$Sv) TO TECHNICIAN FROM SYRINGE AND PATIENT

| | Syringe | Patient |
|---|---|---|
| Bone | 0.61 | 1.16 |
| Liver | 0.09 | 0.12 |
| Kidney | 0.38 | 0.42 |

The data are for dispensing, injecting and imaging with a single dose of radiopharmaceutical.

was in the syringe tends to be disregarded in many departments. We have made some dose measurements encompassing dispensing, injecting and imaging of patients (Table III) for bone, liver and kidney studies. It can be seen that the patient contributes a greater irradiation dose to the technician/radiographer than does the syringe for each of these types of study. This does not mean that one should ignore clinical care of the patient, but it does, for example, mean that when talking to an injected patient, one should keep at a reasonable distance, for example greater than 1 m

### IMAGING ROOMS

In imaging rooms the presence of a patient alone does not require a controlled area because of the exemptions in Table I, B. However, if injections are given in the room, the considerations of the injection area become relevant, and a controlled area is required. Some patients would of course have accompanying nurses and they will enter the controlled area under a written system of work, as previously described. The only particular problem which arises is the handling of gamma-camera flood sources. They are held for a very short time each day, but the surface dose rate at the edge of a $^{57}$Co source is approximately 500 $\mu$Sv per h, well above the limit described in the *IRR* Para. 6(5)a for direct manipulation by the hand. To comply with the *IRR*, gloves should be worn.

### WAITING ROOMS

Patient waiting rooms present an interesting problem. If the 150 MBq MeV limit in Table I, B, is not exceeded, a controlled area is not required. However, most departments will have several patients in their waiting room and the limit will be exceeded. Dose rates from patients have been reported from my department; the worst example, for a bone scan patient, is 13 $\mu$Sv per h at 0.5 m and 3.4 $\mu$Sv per h at 1 m. We have taken the view that the waiting area should be a controlled area and those entering it should be under a written system of work; in practice this is not inconvenient. However, others have suggested that patients and their accompanying nurses or relatives should be kept 1 m apart by screwing aspidistras to the floor.

### WARDS

In the ward a single patient is exempt from requiring a controlled area (Table I, B). If patients are injected on the ward, a temporary controlled area is required, but this does not require physical demarcation, and a description of any such controlled area can be kept in the sister's office. Collection of urine is a problem. If the urine is kept for more than 24 h and the activity exceeds, for example, 5 MBq $^{99}$Tc$^{m}$ or 0.05 MBq of $^{131}$I (*IRR* Schedule 2), then it is a source which must be labelled and accounted for. To avoid colleagues having to come in at weekends and bank holidays, we feel that a label issued by the nuclear medicine department indicating that the activity does not exceed a certain level will comply with this regulation.

There is little published information on dose rates to ward nurses but we have made some estimates based on the time that the nurse spends with the patient. The details are described in Harding et al (1986b) and show that even if the patient had an investigation very early in the morning, the dose to the nurse would not generally exceed 20 $\mu$Sv in a day. The exception would be the patient who had been injected with a large amount of activity, for example a bone scan patient, and who was totally or partially helpless. The sort of exposure under these circumstances would be 99 $\mu$Sv and 44 $\mu$Sv, respectively, per day. An enthusiastic nurse who worked every day for a month and had one helpless patient every 3 days would not reach the monthly dose limit! However, it is important to note that the factors contributing most to the higher dose rates are incontinence and catheter care, treatment of pressure areas, and feeding the patient. However, I would emphasise that, in the case of ward nurses, the main protective factor is that they would rarely look after a patient who had had a radionuclide investigation and was so ill. Most of our patients walk into the department and represent minimal hazard when they go back to the ward.

### THERAPEUTIC DOSES

Two other procedures which might take place in the nuclear medicine department are administration of $^{32}$P, or $^{131}$I for thyrotoxicosis. We were particularly concerned that the *IRR* might create a situation where such patients have to be admitted, contrary to current practices. In the case of radioactive phosphorus, the area in which the phosphorus is administered needs to be a controlled area, but after injection there are no restrictions on the patient because there is only beta emission. In the case of radioactive iodine used for the treatment thyrotoxicosis, the situation is a little confused. In my department we use standard doses of either 200 MBq of $^{131}$I in the routine case, or 600 MBq in the patient who is in heart failure or for any other reason requires to be controlled effectively. Our data show that at 0.5 m from a patient who has had 600 MBq of iodine, the time-average dose rate is 60 $\mu$Sv per h. Exemption from a controlled area could therefore be invoked using *IRR* Schedule 6, Section 3c, as long as no one comes closer than 0.5 m to the patient. It is anticipated that the *Notes for Guidance* will remain essentially unaltered and will recommend that following 125 MBq of iodine there should be no restriction on the patient travelling home, up to 500 MBq they may travel home on public transport as long as their journey does not exceed an hour; if they travel other than by public transport then the limit is 1000 MBq. Clearly, some such provision is required because it is inconceivable that we would have to change totally the practice of medicine, so that patients who have been given iodine for thyrotoxicosis had to be kept in hospital.

### SPILLAGES

A situation which sometimes causes anxiety is what to do if a patient is incontinent, or staff drop a syringe or a bottle containing radioactive substances. The procedure is quite simple and unchanged. The first point to bear in mind is to attend to any urgent needs of the patient and inform the Radiation Protection Supervisor. Gloves and gowns should be worn, and the mess should be cleared up, whatever this mess constitutes (urine, vomit, broken ampoule) Having made the patient or the floor socially clean, an assessment of contamination should be made and, if necessary, decontamination agents used. What must be avoided is the panic reaction of scrubbing everything in sight, including the patient or the member of staff, thereby increasing skin permeability to any possible contamination.

### WOMEN'S PROBLEMS

There are three matters relating to women which have to be considered, firstly the "10-day rule". The 10-day rule has been removed from the *ARSAC* document. However, the so-called "28-day rule" (*Exposure to Ionising Radiation of Pregnant Women)* (DHSS, 1985) specifically excludes administration of radioactive substances to patients and we await the corresponding guidance for nuclear medicine. Hopefully this will not be inconsistent with the previously quoted document.

The question of patients who are breast feeding and who have to have nuclear medicine investigations has been subject to arbitrary rules. The paper by Ahlgren et al (1985) and the editorial by Coakley and Mountford (1985) give details of the excretion of pharmaceuticals in breast milk. The data show that in the case of $^{99}\text{Tc}^{\text{m}}$ DTPA, MDP, or labelled blood cells, the milk from only one feed need be discarded. In the case of other technetium radiopharmaceuticals and iodine-labelled hippuran, the milk from three feeds should be discarded. As milk has to be discarded, patients will usually be prepared to bring it to the hospital so that it can be checked for radioactivity and more data can be acquired. Other radiopharmaceuticals have to be considered individually. The patient should, in addition, be advised to avoid close contact with the child, and it is necessary to record the instructions given in the patient's notes or on the patient's record card.

Lastly, I hope that the revised *Notes for Guidance* will not contain the statement that patients treated with radiopharmaceuticals "should not share the same bed as the spouse". This comment is inapt, or possibly naive!

### CONCLUSIONS

The new regulations and guidance on radiation protection are unlikely to have a marked effect on practices in well run nuclear medicine departments. However, there are still several areas in which detailed multidisciplinary discussion will need to take place. At hospital level, the natural forum is the radiation safety committee, which comprises physicists, radiopharmacists, nuclear medicine consultants, radiologists, radiographers, clinical chemists and nurses

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1987, *The British Journal of Radiology*, 60, 919–922 SEPTEMBER 1987

# The application of cost–benefit analysis when considering action to reduce environmental dose rates in hospitals

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*(Received February 1987 and in revised form April 1987)*

ABSTRACT

Cost–benefit analysis, in which a monetary value is assigned to radiation-induced health detriment, is used to establish whether a proposed course of action to reduce the dose rate in a particular environment is reasonable in the "as low as reasonably achievable" context. The instantaneous dose rate is used in conjunction with a use factor and a man-occupancy factor to establish a dose accumulation rate. This, in turn, is used to calculate what capital expenditure on radiation protection measures is reasonable Such an approach provides an objective method of assessing and comparing radiation protection problems and leads to better consistency in allocating available resources.

The *Ionising Radiations Regulations* (1985) are concerned with ionising radiation arising from any work activity. They are statutory requirements, approved by Parliament, and in force throughout the United Kingdom. Amongst other things, they require every employer to take all necessary steps to restrict, so far as reasonably practicable, the extent of which his employees and other persons are exposed to ionising radiations. This idea is not new and is often referred to as the ALARA principle, following the wording used by the International Commission on Radiation Protection (ICRP, 1965) which recommended that doses to personnel are not only kept below prescribed limits but are also kept "as low as readily achievable, economic and social factors being taken into account". In more recent publications (ICRP, 1977) the word "readily" has been replaced with the word "reasonably". Whenever possible the employer is to achieve this restriction by means of engineering controls and design features which include shielding, etc., rather than by operative procedure control. It is the duty of the Radiation Protection Adviser (RPA) to give the employer expert advice in order that the employer may fulfil his obligations under the requirements of the *Ionising Radiations Regulations*, and part of that advice will be on whether or not significant capital expenditure, on building work for example, or on the purchase of additional shielding materials, is reasonable within the ALARA context. Without applying some appropriate measure of "reasonableness" such advice will inevitably be highly subjective and will be in danger of being inconsistent.

In cost–benefit analysis a monetary value is assigned to radiation-induced health detriment. Hence a cash equivalent of preventing or reducing population exposure to ionising radiations can be calculated and compared with the actual costs that would be incurred in achieving a particular result. Within the United Kingdom the National Radiological Protection Board (NRPB) has advocated the use of cost–benefit analysis as an aid to decision-making in radiation protection and published two consultative documents on the subject (NRPB, 1980, 1982). In these consultative documents a very high financial benefit was assigned to preventing or reducing collective doses made up of higher individual doses, and particularly high weightings were applied as individual doses approached the dose limits. Recently a leaflet in the Advice on Standards of Protection series (ASP9) has been published (NRPB, 1986) in which the Board again expresses its support of cost–benefit analysis. In this publication, however, the very high weightings suggested earlier have been considerably reduced.

Let us suppose that the environmental dose rate in, or close to, an existing radiation facility is sufficiently high to require consideration. The RPA must now advise on a "reasonable" course of action. The purpose of this paper is to discuss how cost–benefit analysis, and the formal advice given by the NRPB in ASP9, can help to ensure that the advice given is objective and consistent with that given in other, similar situations.

## METHOD OF ASSESSMENT

The RPA will be alerted to a possible problem when the instantaneous measured dose rate in a given area is reported as being relatively high. In order to estimate what effect this will have on the integral population dose he will need information about the occupancy of the area and need to know whether the measured dose rate is continuous and constant, or whether it changes with the use of a particular item of equipment in the vicinity. These additional considerations can be taken into account by defining a dose accumulation rate, obtained by multiplying the instantaneous dose rate by a man-occupancy factor and a use factor, thus:

$$\text{dose accumulation rate} = \text{instantaneous dose rate} \times \text{man-occupancy factor} \times \text{use factor}$$

The dose accumulation rate is the averaged rate of accumulation of integral population dose due to the exposure of personnel in the area in question and has units of man-$\mu$Sv $h^{-1}$. For the present purposes 100% occupancy is defined as 168 man-h per week, and hence an office occupied by one person during a 37 h working week will have 22% occupancy, whereas a nursing station manned round the clock by an average of two people for 7 days a week will have 200% occupancy. In most cases the use factor is the fraction of time that the equipment causing the high dose rate is in use while the area in question is occupied. Alternatively one may start by establishing a use factor and then consider occupancy during use periods. However, some care will be necessary if the dose rate is intermittent or variable during occupancy periods, since the two may not be coincident.

A continuous and constant dose rate of 1 $\mu$Sv $h^{-1}$ in an area of 100% occupancy contributes $8.76 \times 10^{-3}$ man-Sv to the annual population dose, and hence the contribution to the population dose from a dose accumulation rate of $E$ man-$\mu$Sv $h^{-1}$ will be $E \times 8.76 \times 10^{-3}$ man-Sv. In order to convert this into an equivalent annual cost it is necessary to multiply by the cash equivalent of 1 man-Sv, say £$Q$, and hence the equivalent annual cost of such exposure is £$Q \times E \times 8.76 \times 10^{-3}$.

Any measure taken to reduce the dose rate, and therefore reduce the equivalent annual cost, will remain effective over a period of years and it would therefore be unreasonable to compare the capital cost of introducing such a measure with the dose reduction achieved in just 1 year. An additional factor has therefore to be introduced to convert a recurring annual cost into a single capital cost. The value of such a factor will depend on the amortisation period and the annual discount rate thought to be appropriate. A factor of eight corresponds to amortisation over 12 years at 7% and adopting this we have:

$$\begin{aligned}\text{maximum reasonable capital expenditure}\\ &= £Q \times E \times 8.76 \times 10^{-3} \times 8\\ &= £Q \times E \times 0.07\end{aligned}$$

This is the maximum reasonable capital expenditure to reduce the dose rate to zero, and will be proportionally less if only partial reduction of the dose rate is effected. For example, the maximum reasonable expenditure on incorporating an additional half-value thickness of shielding will be £$Q \times E \times 0.035$.

### THE CASH EQUIVALENT, £$Q$, OF 1 MAN-SV

The NRPB (1986) now recommends that, in the United Kingdom, a baseline value of £3000 per man-Sv is adopted for the years 1985–89, to reflect the costs of additional health care, loss of output, etc., arising from radiation-induced health problems. The NRPB also recommends that the baseline cost be multiplied by a factor between one and 16 where the integrated population dose is made up of higher individual doses. This implies that it is right and justifiable to spend more money on protecting those individuals who are at higher risk The present advice is that in protecting members of the public, where the legal dose limit of 5 mSv per annum applies, then in most circumstances a figure of £5000 per man-Sv can be adopted, and for radiation workers, operating to the higher legal limit, a general figure of £15 000 would be more reasonable, implying multiplying factors of 1.2 and 5. Using the equations discussed above, the two suggested cash equivalents correspond respectively to £350 ($0.07 \times £5000$) and £1050 ($0.07 \times £15\,000$) reasonable capital expenditure for each man-$\mu$Sv $h^{-1}$ reduction in dose accumulation rate.

The earlier consultative documents (NRPB, 1980, 1982) suggested a banded structure, with large discontinuities in the equivalent costs where individual doses were known to exceed certain levels. In many ways this was better because, in addition to the aspects of actual radiation risk, it also reflected the extra administrative effort required, and the considerable political and emotional pressures that are brought to bear when certain threshold annual dose levels are exceeded. Perhaps the most obvious of these is the $\frac{3}{10}$ maximum permissible dose for radiation workers, where an increase in annual dose from 14.5 mSv to 15.5 mSv causes problems totally out of proportion to the corresponding increase in risk. Similar discontinuities occur where individual doses exceed 5 mSv and 1 mSv per annum The NRPB states, with considerable emphasis, that its current suggested framework is not intended to cover all considerations affecting decisions on radiation protection requirements. It is therefore up to the individual RPA to decide how any additional considerations are taken into account, and one way of doing this would be to incorporate additional multiplying factors into the NRPB framework, particularly to take note of the various threshold levels. The scheme suggested here for assessing reasonable capital expenditure, detailed in Table I, is based on the NRPB advice but includes extra factors, admittedly very subjective, which recognise the discontinuities at individual dose thresholds.

### EXAMPLES

Suppose a remote afterloading machine is installed in a hospital side ward and the averaged measured instantaneous dose rate in an adjoining room is 45 $\mu$Sv $h^{-1}$ when the equipment is in use, which may be for up to 120 h per week. The time-averaged dose rate is therefore greater than 7.5 $\mu$Sv $h^{-1}$ and consequently the room will be a controlled area and a written system of work will apply for any activity therein. The question remains: is it reasonable to implement engineering controls or erect shielding to reduce the instantaneous dose rate and, more particularly, what capital expenditure on such an exercise would be reasonable?

In this example, usage corresponds to a use factor of 0.71 (120/168) and if the occupancy during the time the

TABLE I

MAXIMUM REASONABLE CAPITAL EXPENDITURE FOR EACH MAN-$\mu$Sv H$^{-1}$ REDUCTION IN DOSE ACCUMULATION RATE*

| Individual annual dose band (mSv) | Maximum reasonable expenditure per man-$\mu$Sv h$^{-1}$ reduction |
|---|---|
| <1 | £350 |
| 1–5 | £2000 |
| 5–15 | £3000 |
| 15–50 | £5000 |

*Effective 1985–89.

equipment is in use is, say, 6 man-h per day, then the man-occupancy factor is 0.25. Hence the dose accumulation rate = $45 \times 0.71 \times 0.25 = 8$ man-$\mu$Sv h$^{-1}$. If staff doses, as recorded on their personal dose monitors, suggests that they will exceed the $\frac{3}{10}$ limit for occupationally exposed persons, then the maximum reasonable capital expenditure on reducing the dose rate to zero, based on the figure in Table I, would be $8 \times$ £5000 = £40 000 or, alternatively, incorporating an additional half-value thickness of shielding material would be regarded as reasonable if it could be done for less than £20 000.

If, on the other hand, the average measured instantaneous dose rate were 25 $\mu$Sv h$^{-1}$ and personnel monitoring suggested that no member of staff would, in fact, under the circumstances already prevailing, exceed the $\frac{3}{10}$ limit, but that most would exceed the $\frac{1}{10}$ limit, then the maximum reasonable sum of money to spend on reducing the dose rate to zero would be £13 000 [ = $(25 \times 0.71 \times 0.25) \times 3000$] and only half of this for a reduction in dose rate by a factor of two.

In a more complex situation a particular practice may result in different dose rates in different areas and contribute to doses accumulated by different groups of people. Consider a ward where a patient is being nursed following $^{137}$Cs needle implant of the tongue, and where no bedside shielding is used. The dose rate at the bedside may be, say, 100 $\mu$Sv h$^{-1}$, and elsewhere on the ward it perhaps averages 2 $\mu$Sv h$^{-1}$. If five such patients are nursed on this ward in the course of 1 year, and the average duration of each implant is about 1 week, then the use factor is 0.1 (= 5/52). Suppose that staff attendance at the bedside averages 0.5 man-h per day, then the man-occupancy factor in the 100 $\mu$Sv h$^{-1}$ area is 0.02 (= 0.5/24). Elsewhere the average number of staff members on the ward at any time may be three, and hence three is the man-occupancy factor to be used in calculating the dose accumulation rate in the 2 $\mu$Sv h$^{-1}$ area. Each area then has associated with it a dose accumulation rate of:

$$0.2 \text{ man-}\mu\text{Sv h}^{-1} = 100\ \mu\text{Sv h}^{-1} \times 0.1 \times 0.02$$
$$\text{and } 0.6 \text{ man-}\mu\text{Sv h}^{-1} = 2\ \mu\text{Sv h}^{-1} \times 0.1 \times 3$$

It is interesting to note that, in this example, the dose accumulation rate in the area of low instantaneous dose rate is three times that in the high dose rate area as a result of the man-occupancy factor assigned. If doses recorded by ward staff fall into two costing groups, say above and below 15 mSv per annum, then the capital cash equivalent will have to be calculated as the sum of two components, one for each group. To do this, the dose accumulation rate is divided into the same proportions as there are personnel in each group. In the present example suppose 15% of relevant personnel record annual doses above 15 mSv and the remaining 85% record annual doses below this figure. Then, using the figures in Table I, the capital cash equivalent of totally shielding the high dose rate area at the bedside will be:

$$0.2 \times [(0.15 \times £3000) + (0.85 \times £2000)] = £430$$

Similarly, the capital equivalent of totally eliminating the low dose rate elsewhere on the ward would be three times this figure, viz. £1290. In practice a proposed course of action, such as the use of bed shields, will not be 100% effective and may well have a different effectiveness in the different areas. These cash figures will therefore have to be reduced according to the expected dose rate reduction in each area.

Further components to the total capital equivalent may be calculated by considering dose accumulated by visitors and dose accumulated by other patients. Whether or not it is justifiable to include the latter may depend on whether or not such patients are receiving radiation therapy, and on their average life expectancy. If visitors are costed at the level corresponding to the lowest costing band in Table I, their component will be small, even though the man-occupancy factor may be relatively large, owing to the number of people involved.

In general, the capital equivalent of any particular proposed course of action will be the sum of the capital equivalents of all separate components.

## CONCLUSIONS

Clearly, the valuations cannot be precise and, if the method is adopted, individual RPAs may well wish to make further adjustments to account for local circumstances. However, the calculations are very easily done and will serve to highlight particularly bad radiation protection problems, and will equally help to prevent vast over-reaction to problems which are more emotional than real. More important is the facility that the analysis provides for comparing radiation protection problems which should in turn lead to objective judgments on priorities when allocating available resources. Further, if this type of analysis is followed, then all advice given by the RPA will at least be self consistent.

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# Book review

*Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields* NCRP Report No 86, pp. xii+382, 1986 (NCRP, Maryland), $20.
ISBN 0-913392-80-4

The first report by the National Council on Radiation Protection and Measurements (NCRP) on radiofrequency electromagnetic (RFEM) radiation was published in 1981 (Report No 67) Report No. 86 is the second report and has been prepared by Scientific Committee 53 on Biological Effects and Exposure Criteria for RFEM Radiation. The report addresses the biological effects of exposure to RFEM fields in the frequency range $3 \times 10^5$ Hz to $10^{11}$ Hz. It has 17 chapters with subjects such as interaction mechanisms with biological materials, macromolecular and cellular effects, chromosomal and mutagenic effects, there are sections on RFEM effects on reproduction, growth and development, interactions with the haematopoietic and immune systems as well as interactions with the endocrine and nervous systems, other subjects include behavioural studies, epidemiological studies on human beings and medical applications. The final chapter is on exposure criteria and rationale.

It is emphasised repeatedly that temperature is a critical variable which must be considered in any experimental work with RFEM fields Irradiation at non-thermogenic levels (*e g* at specific absorption rates below 1 W/kg at frequencies of 300 kHz–300 GHz) results in few, if any, unequivocal effects on the haematopoietic or immune systems of laboratory animals However, under some experimental conditions (*e g.* irradiation with pulsed RFEM fields) lymphocyte populations may be affected. The effects of RFEM fields on endocrine function are considered to be generally consistent with responses to thermal input and to non-specific stress, which can also arise from thermal loading Irradiation of the cardiovascular system, the blood–brain barrier and the nervous system are also considered Whereas exposure to fields at low levels (less than 10 mW/cm$^2$ or less than 2 W/kg) for short periods of time does not appear to cause significant cardiovascular effects and the blood–brain barrier is not affected adversely, long-term exposure studies are inadequate to justify firm conclusions

Evidently, behavioural studies provide a highly sensitive index of field–body interactions with a broad spectrum of end-points A single pulse of RFEM energy can be heard by human beings and laboratory animals; the threshold of perception is but a few mJ/kg of body mass, whereas the threshold of convulsive activity requires absorption of energy six orders of magnitude greater For acute exposures, specific absorption (SA) and specific absorption rate (SAR) thresholds are often remarkably stable within animals of a species, but interpretation of the implications of altered behaviour remains controversial.

Studies of human beings include epidemiological studies of US Naval personel occupationally exposed to radar and also of American Embassy personnel in Moscow suspected of RFEM irradiation. In both these groups no significant adverse effects were detected that could be attributed conclusively to the exposure

Thermal regulation responses in humans are described and the value of mathematical simulation emphasised. Although some general characteristics of the thermo-regulatory responsivities to RFEM irradiation may be derived for animal studies, it is stated that the need for psycho-physical behavioural and physiological investigations of human subjects remains

The chapter on exposure criteria and rationale summarises information on key end-points that are useful in establishing exposure criteria In the frequency range 30 kHz–300 MHz, behavioural disruption appears to be the most significant end-point that occurs at the lowest SAR and within a relatively narrow range of whole-body averaged SARs ranging from 3 to 9 W/kg A safety margin of ×10 has been applied for occupationally exposed populations This gives an equivalent far-field power density of 1 mW/cm$^2$, a value that limits the maximum whole-body averaged SAR to a level below 0 4 W/kg (averaged over any 0.1 h period). Furthermore, it is recommended that there be an average exposure criterion for the general public that is set at a level equal to one fifth that of occupationally exposed individuals (*i.e* 0.08 W/kg). This is to be averaged over a time period of 0.5 h to accommodate special circumstances for the public at large, such as the passage by the individual past high-powered RFEM sources The recommendations for occupational exposures beyond 30 kHz–300 MHz are more complex and rise to power density levels of 100 mW/cm$^2$ at low frequencies and 5 mW/cm$^2$ at high frequencies These criteria are discussed in relation to American National Standards Institute (ANSI) 1982 criteria and other international recommendations

Report No 86 provides an encylopaedic list of references (about 950 in total) and data on the biological effects of exposure to RFEM fields The assessment of published work is balanced and the relevance of data to safety studies is presented clearly. This report is essential reading for anyone embarking on experimental work with RFEM fields and will be a useful reference for all who are interested in safety

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1987, *The British Journal of Radiology*, *60*, 923–924 SEPTEMBER 1987

# Technical note

## Peripheral angiography in a standard fluoroscopy room

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The arrival of digital subtraction angiography, whilst a boon for much peripheral angiography, does produce problems. The new equipment takes several months to install and, when installed, may break down more often than the simpler equipment it replaces It is therefore useful to have a back-up system. Most hospitals cannot justify two angiographic rooms and therefore the back-up usually has to be with equipment used for other purposes.

In order to overcome the problem of a fairly large workload with no available angiographic facilities we learned the use of stationary angiography using a screening room and a mobile X-ray machine.

### TECHNIQUE

The patient is placed supine with the knees tied together and pads under the thighs and ankles to enable a quick cassette change. Two preliminary radiographs are taken: one of the lower abdomen and pelvis, using the overcouch tube and the Bucky; the other of the lower legs from the ankles up, using a mobile X-ray machine (Todd Research Triton).

The catheter is placed in the aorta by the normal Seldinger technique using the undercouch tube of the normal fluoroscopy set. The overcouch tube is then positioned over the pelvis and a 43 cm × 35 cm cassette placed in the Bucky. A similar-sized cassette is placed directly under the lower legs with the ankle joint at the lower edge of the film, and the mobile tube positioned over it (Fig. 1) The cassette is usually long enough to include the knee on this view. Concentrated low-osmolar contrast medium (iopamidol 370) is placed in the injection pump and 50 ml of this is injected at a speed of 8 ml/s. This produces a long column of reasonably concentrated contrast medium and allows two injections without refilling the pump. The long column allows a greater margin for error in the timing of the exposures.

The radiograph of the lower abdominal aorta and pelvic vessels is taken 5–6 s after the start of the injection The first radiograph of the lower leg is taken from 10 to 15 s after the beginning of injection, depending on the radiologist's view of the likely speed of flow of contrast medium. Twelve seconds proved to be a good compromise, but occasionally it may be necessary to be slightly quicker than this, *e.g.* when some of the lower leg pulses are present. A greater delay may be used if the flow appears to be extremely slow when the contrast medium is injected during the positioning of the catheter under fluoroscopic control.

The lower-leg cassette is removed as quickly as possible after the first film is exposed and replaced by a second and then a third cassette. With one person removing the cassette while another replaces it, it is possible to take the third radiograph about 25 s after the start of the injection of contrast medium. A mobile machine is required which can recharge for a further exposure in about 3 s. A second injection of contrast medium must now be made in order to obtain radiographs of the vessels in the thigh This is achieved by using the overcouch tube and the Bucky (Fig. 2). The timing of the exposure after the start of injection of contrast medium can be judged from the previous radiographs, but 9–10 s is the usual time. If 35 cm × 43 cm cassettes are used it is almost always possible to get at least 5 cm of overlap on adjacent radiographs.

Occasionally the first radiograph of the lower leg may not, for some reason, be acceptable. We have managed to take a repeat view of this area during the second injection of contrast medium by moving the Bucky out of the way very rapidly before placing the cassette under the lower leg for exposure by the mobile machine. The lower-leg radiographs are numbered by lead figures on the cassettes to facilitate identification.

### RADIATION DOSIMETRY

Measurements were made of the radiation doses received by the patient and by staff changing the

TABLE I

RADIATION DOSES RECEIVED BY THE PATIENT

| | X-ray exposure | Total skin dose (mGy) | Energy imparted (mJ) |
|---|---|---|---|
| Abdomen | 75 kV 1 mAs<br>(5 min) | 100.00 | 3.2 |
| Abdomen | 85 kV 32 mAs<br>(two exposures) | 7.80 | 48.0 |
| Thighs | 70 kV 25 mAs<br>(one exposure) | 2.20 | 11.7 |
| Legs | 50 kV 6 mAs<br>(four exposures) | 0.80 | 3.2 |

Effective whole-body dose (patient) = 2.30 mSv per investigation.

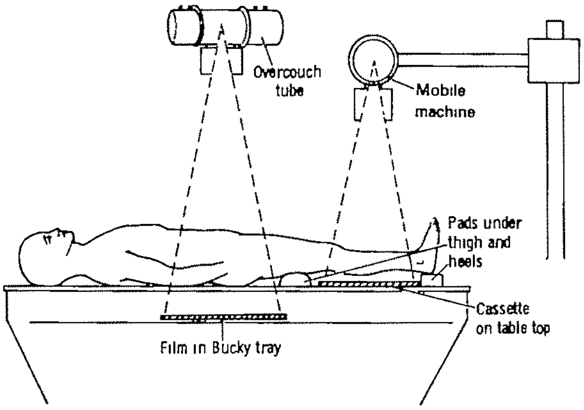

Fig 1
Position for pelvic and lower-leg vessels

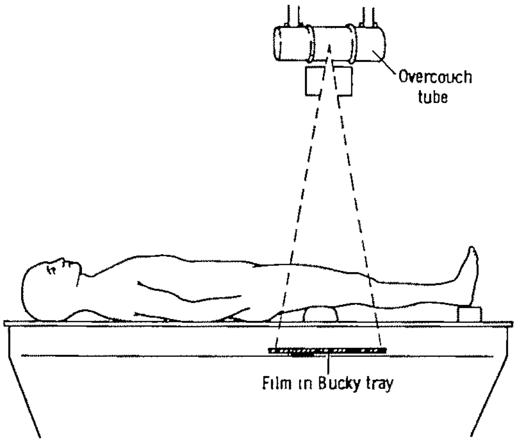

Fig 2.
Position for thigh vessels

cassettes The patient doses are given in Table I These compare favourably with those received from conventional angiography, partly because fewer exposures are used.

The scattered doses received by staff are shown in Table II. The dose of radiation due to the radiographic exposures to those changing the cassettes is small. It is assumed that lead aprons were worn and that staff stood back to a distance of 2 m during the actual exposures It is evident that the scattered dose to the radiologist is almost entirely due to the fluoroscopy, which is similar in a specialised angiography room. The technique was used eight to 10 times per week in our department for a 6-month period. During this time no significant dose was recorded on the staff's personal film badges.

## DISCUSSION

Peripheral angiography in the fluoroscopy room is not new, but there are few reports of its use. Increasing numbers of radiologists have been brought up with only high technology, and it is tempting to say that it is not possible to examine patients if complicated machines are not working. However, many peripheral angiograms can be performed in the simple manner described above. The delicate manoeuvring of a guide-wire or catheter through difficult iliac vessels can be slightly cumbersome, as the fluoroscopic tube and film carriage of most screening sets are rather large, making the radiologist stretch in order to reach the groin. The quality of the radiographs taken with the Bucky are excellent, but those of the lower limb taken with the mobile machine may lack contrast. The whole procedure is made easier if a team of four can be assembled during the actual taking of the radiographs and obviously there is less latitude in timing when only one radiograph of a particular area is possible from each injection of contrast medium. Nevertheless, the examinations are performed just as quickly as those in the angiography room, the costs are certainly no greater than a normal Puck run, and we have had no additional complication.

ACKNOWLEDGMENT

We are very grateful to Mrs A. Dixon-Brown and the Department of Radiation Physics, Churchill Hospital, Oxford for their help with radiation dosimetry.

TABLE II
RADIATION DOSES RECEIVED BY THE STAFF

| | Radiographic procedures | | Radiographic and fluoroscopic procedures | |
|---|---|---|---|---|
| | Skin dose ($\mu$Gy) | EWBDE* ($\mu$Sv) | Skin dose ($\mu$Gy) | EWBDE* ($\mu$Sv) |
| Staff at 2 m from patient | | | | |
| (i) wearing no Pb apron | 0.20–1.5 | – | 20 | – |
| (ii) wearing Pb apron | 0.01–0.10 | <0.5 | 1.5 | 10.0 |
| Radiologist† | 0.01–0.10 | <0.5 | 25 | 150.0 |

*EWBDE = Effective whole-body dose equivalent.

†Wearing a Pb apron and at 2 m from patient for radiographic exposures but 50 cm from X-ray beam centre for fluoroscopic procedures

1987, *The British Journal of Radiology*, 60, 925–928 SEPTEMBER 1987

# Case reports

## Unusual disco-vertebral changes in Gaucher's disease

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The clinical manifestations of non-neuronopathic or chronic Type I Gaucher's disease result from the progressive deposition of glucocerebroside in the reticulo-endothelial cells of the bone marrow, spleen and liver. The pathological changes in both the axial and appendicular skeleton produce a spectrum of radiological features which includes osteoporosis, osteolytic lesions, osteonecrosis, osteosclerosis and modelling deformities (Amstutz & Carey, 1966; Silverstein & Kelly, 1967; Greenfield, 1970).

This case report presents features in the axial skeleton that have not previously been described. Possible pathogenetic mechanisms are also discussed.

### CASE REPORT

A 37-year-old non-Jewish lady with histologically proven Gaucher's disease was admitted for multidisciplinary investigation prior to proposed bilateral total hip replacements. Apart from hypersplenism necessitating splenectomy and a pathological transcervical femoral fracture, the patient had remained in good health until her mid-twenties. Since that time, progressive painful limitation of movement in both hips and similar, but less marked, symptoms in both knees and the dorsilumbar spine had produced considerable disability and loss of mobility.

Examination confirmed the presence of a splenectomy scar. There was severe restriction of all hip movements and, to a lesser extent, knee movements. Although spinal alignment was normal, there was considerable reduction in the range of movement in the dorsilumbar region.

There was abnormal red blood cell morphology consistent with a previous splenectomy and biochemical analysis revealed elevation of the serum acid phosphatase at 12.9 IU/l (normal less than 4 IU/l). Urine analysis, including Clinitest and chromatography, was normal.

Radiographic examination showed changes consistent with advanced Gaucher's disease in both the appendicular skeleton (Fig. 1) and pelvis (Fig. 2). Radiographs of the spine, however, revealed some unusual features. There was almost complete loss of the intervertebral disc spaces in the dorsilumbar region with prominent "vacuum" phenomena and cartilaginous node formation at the lumbar levels (Fig. 3). The lower dorsal and lumbar vertebral bodies were taller than normal and had an abnormal square configuration secondary to loss of the anterior concavity and there was anterior vertebral body synostosis at three levels from D12 to L2 with calcification of the intervening narrowed disc spaces (Fig. 3). Two mid-dorsal vertebrae demonstrated central "step-like" depressions of their end-plates, producing an "H"-shaped configuration (Fig. 4). Computed tomography clearly demonstrated the nature and extent of these bony changes and, in addition, revealed marked degenerative changes in the lumbar apophyseal joints (Fig. 5), and partial fusion of both sacroiliac joints (Fig. 2B).

### DISCUSSION

The most common spinal manifestation reported in Gaucher's disease is that of collapse of one or more vertebral bodies with intact or only slightly diminished intervening disc spaces (Kulowski, 1950; Greenfield, 1970; Myers et al, 1975). By contrast, the striking disco-vertebral abnormality seen in our patient is that of widespread disc destruction and vertebral-body overgrowth. Attention has not been previously drawn to these features although similar changes are apparent in the illustrations of a case described in an article by Rourke and Heslin (1965), indicating that it is not an isolated variant and therefore merits more detailed consideration. The lower dorsal and lumbar vertebral bodies have increased vertical heights when compared with normal values obtained in female patients of

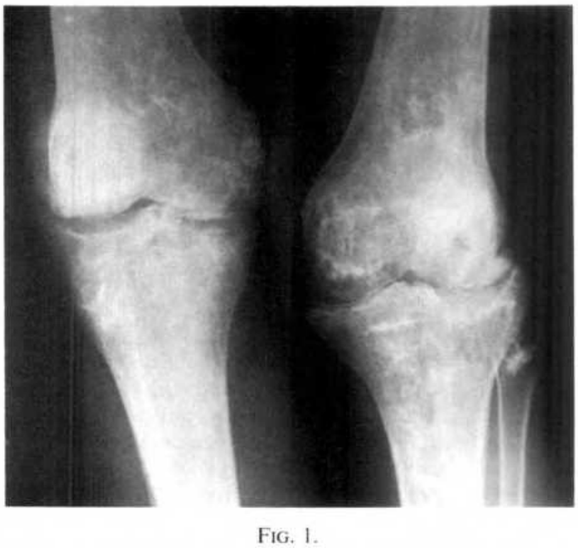


FIG. 1.

Patchy medullary sclerosis due to infarction. The femoral and tibial condyles show evidence of osteonecrosis and there are secondary changes of osteo-arthritis.

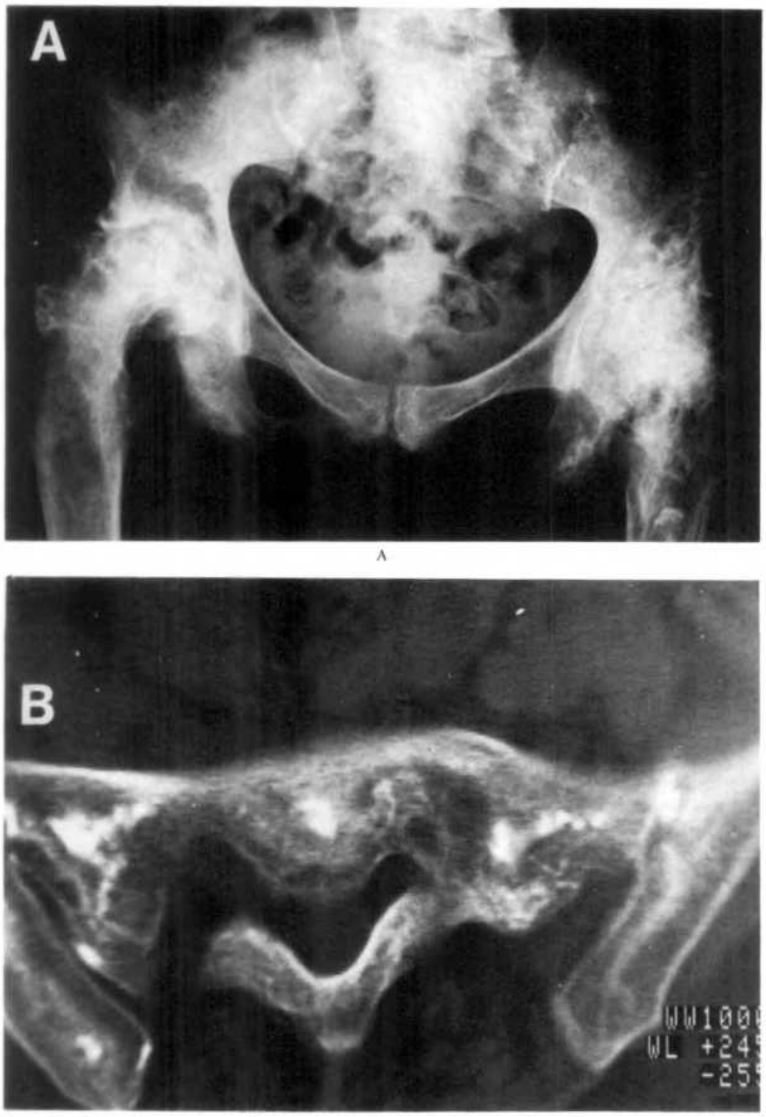


FIG. 2.

(A) Severe collapse of both femoral heads with underlying medullary sclerosis and secondary osteo-arthritis. The sacroiliac joints show partial fusion. (B) Fusion confirmed on CT.

similar age (Hurxthal, 1968). Vertebral growth occurs in a similar fashion to that of any long bone, in that an increase in height results from growth occurring at the upper and lower cartilaginous plates of the vertebral body (Bick & Copel, 1950). In long bones, the rate of growth is influenced by the magnitude of the pressure gradient which exists across the epiphyseal centres, increased growth occurring when pressure is decreased and vice versa (Heuter, 1862; Volkmann, 1869). In the spine the growth of the vertebral bodies interrelates with the intervertebral disc and the growth is affected by the relative forces applied. Thus, observations in children undergoing prolonged spinal immobilisation or posterior fusion procedures suggest that the reduced mechanical forces applied to the vertebral end-plates result in increased vertebral height at the expense of the compressible intervening disc (Risser et al, 1966; McCall et al, 1981). It is conceivable that reduced pressure from the disc due to early degeneration and loss of disc height may alter the forces of growth on the vertebral body in the opposite way. Thus, if the disc degeneration in the present case occurred in childhood during the growth period, it should seem logical that the reduced pressure applied to the end-plates would encourage vertebral overgrowth. The fact that the vertebral heights in the upper dorsal and cervical regions of our patient are normal, with adjacent discs of normal height, would lend support to the concept. The mechanics of early disc degeneration are not clear. Generalised premature disc degeneration is a feature of

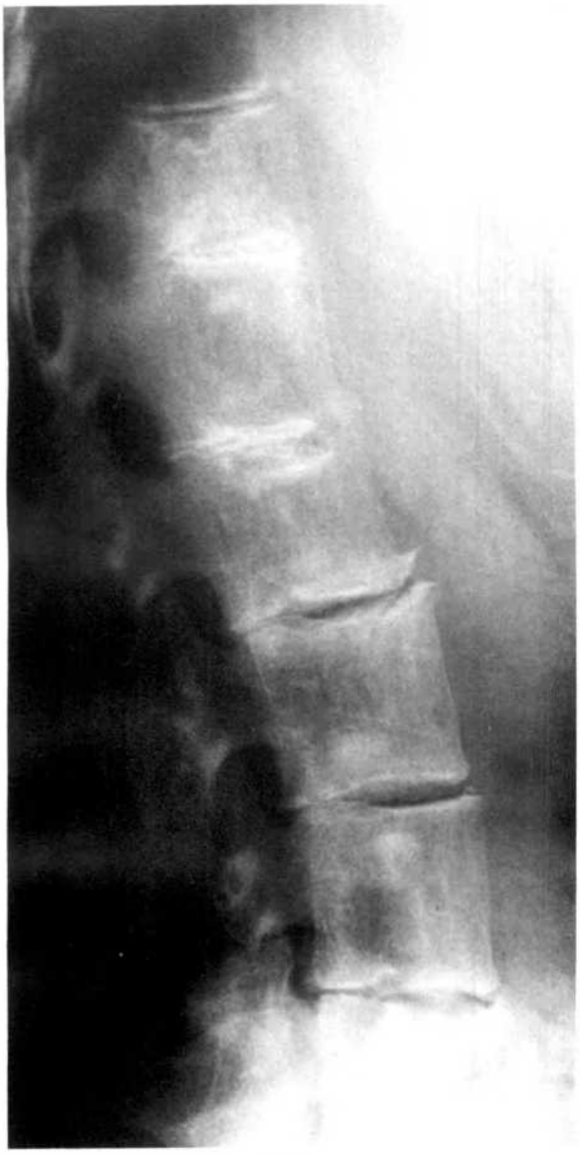
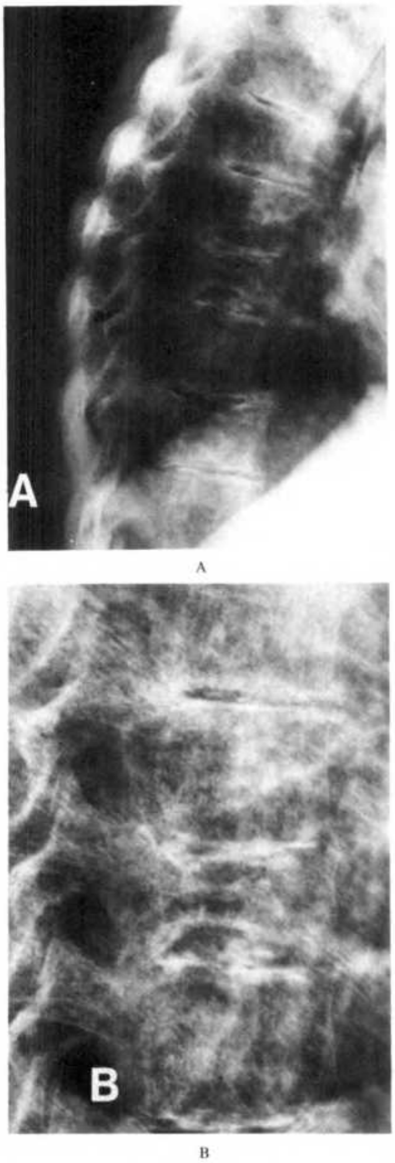


FIG. 3.

The lower dorsal and lumbar vertebral bodies show increased height and squaring of their anterior margins. There is marked disc resorption, with prominent vacuum phenomena and cartilaginous node formation. Anterior vertebral synostosis with calcification of the narrowed intervening discs is demonstrated between D12 and L2.



A

B

FIG. 4.

(A) The lower dorsal vertebral heights are increased and the discs are degenerate. (B) Local view shows in greater detail the morphology of an "H"-shaped vertebral body with collapse of the centre of the end-plate of T9.

ochronosis, but specific biochemical tests on this patient excluded this aetiology. It is possible that the abnormal cellular infiltration seen in other organs in this disease could also occur in the disc, leading to a change in protein and water balance and premature degeneration. Alternatively, interference by glucocerebroside deposition of the integrity of the vascular network in the vertebral end-plate, which is responsible for the passage of nutrients and water to and from the disc, could lead to early degeneration. Compromise of the vascularisation of the end-plate could also be mechanistically related to the central end-plate collapse which produces the "H"-shaped vertebral body. This feature was previously thought to be pathognomic of sickle-cell haemoglobinopathy and its variants and was due to chronic ischaemia causing growth retardation

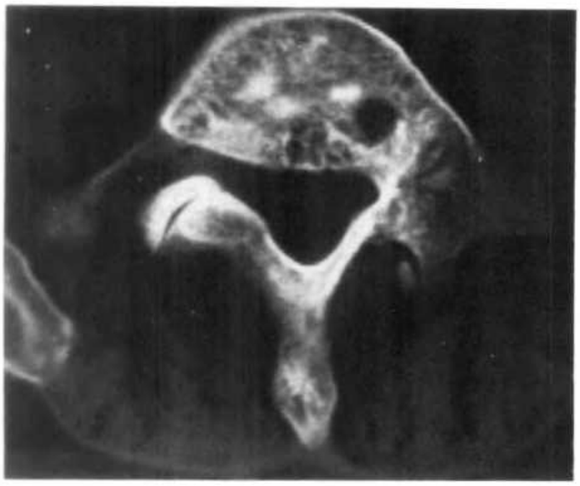


FIG. 5.

Computed tomographic section of the body of L4, showing the altered trabecular pattern, intramedullary infarcts and degenerative changes in the apophyseal joints.

and collapse of the central part of the end-plate. Other authors (Hansen & Gold, 1977; Schwartz et al, 1979) have also recently described this feature in patients with Gaucher's disease although they have ascribed the central depression to a different mechanism, involving initial vertebral-body collapse and subsequent regrowth which has its greatest magnitude at the periphery of the end-plates (Schwartz et al, 1979).

The anterior vertebral synostosis of D12 to L2 closely resembles the changes seen in senile kyphosis and Scheuermann's disease (Schmorl & Junghanns, 1971). In these conditions, the anterior margins of narrowed intervertebral discs undergo further compression and destruction between adjacent vertebral bodies, and bony metaplasia of disc remnants eventually leads to anterior osseous bridging. Given the extent of loss of underlying disc space in our patient, the development of these non-specific intervertebral fusions is hardly surprising.

Finally, the loss of the normal anterior vertebral concavity giving rise to the square-shaped vertebra is almost certainly due to the modelling deformity consequent upon marrow infiltration and new bone formation similar to that seen in the Erlenmeyer flask deformity of the distal femur in this condition.

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1987, *The British Journal of Radiology*, 60, 929–931 SEPTEMBER 1987

*Case reports*

# Hodgkin's disease in a patient with polysplenia

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(*Received July 1986 and in revised form January 1987*)

Polysplenia is a complex congenital syndrome. It forms one part of the spectrum of viscero-atrial situs abnormalities, along with asplenia (Ivemark's syndrome) and situs inversus. Lymphoma has been reported in cases of "ectopic" or "wandering" spleen, but not, to our knowledge, in polysplenia. We report the case of a 42-year-old patient who was a polysplenic with Hodgkin's disease.

## CASE REPORT

A 42-year-old gardener was admitted to another hospital with a 6-week history of ill health, he complained of night sweats, anorexia, lassitude and episodic diarrhoea There was no significant previous medical history

Investigation revealed a microcytic anaemia, with a fluctuating pyrexia, the cause of which could not be established. Cultures (including TB) were negative

What appeared to be an enlarged azygos lymph node on chest radiography was shown to be a dilated azygos vein. Intravenous pyelography and ultrasound examination were thought to show an enlarged right kidney. Empirical antibiotic therapy was unsuccessful

The patient was transferred to our hospital where a repeat ultrasound examination demonstrated an abnormal visceral situs The "enlarged right kidney" was identified as an abnormally located spleen. Computed tomography (CT) demonstrated a central abdominal mass, probably lymph nodes, in addition to multiple spleens (Fig. 1)

The patient remained unwell with spiking temperatures of 104°F and episodes of peripheral and pulmonary oedema.

At laparotomy, in addition to the abnormal situs of the abdominal organs, with malrotation of the bowel, a mass of lymph nodes was found at the base of the mesentery which biopsy showed to be nodular sclerosing Hodgkin's disease

The patient's condition continued to deteriorate and he died shortly afterward Post-mortem examination (Fig. 2) confirmed the presence of multiple spleens, seven in total, together weighing 500 g. The right and left lobes of the liver were approximately the same size and the gallbladder was to the left of the midline. The small bowel occupied the right upper and right lower quadrants, while the large bowel was all to the left of the midline.

The root of the small-bowel mesentery was found to be infiltrated with tumour and the terminal event had been peritonitis, secondary to jejunal perforation.

The lungs were bilobed. The heart was normal and, apart from azygos continuation of the inferior vena cava, the great vessels were normal.

## DISCUSSION

The term "situs" describes the relationship of the atria and the viscera to the midline. The normal condition is situs solitus (left-sided atria, stomach and spleen, right-sided liver). Situs inversus is the mirror-image condition. Situs indeterminus, or ambiguus, describes cases which cannot be so categorised.

Polysplenia is a syndrome with a tendency to bilateral left-sidedness, *i.e.* situs indeterminus with multiple spleens. Asplenia is a syndrome with a tendency to bilateral right-sidedness, *i.e.* situs indeterminus with an absence of spleens (Rose et al, 1975; Tonkin & Tonkin, 1982).

There are a number of possible features in polysplenia (Table I), with considerable variation in frequency. There is no single pathognomonic anomaly, but situs indeterminus and azygos return of the inferior vena cava are common (Arnold et al, 1983). As cardiac malformations are notably less common than in asplenia, survival into adult life is not uncommon. The fortuitous nature of the diagnosis means that the exact incidence of polysplenia is uncertain. In this patient the

TABLE I

POSSIBLE FEATURES OF POLYSPLENIA*

*Abdomen*

Abnormal visceral situs, including hepatic symmetry, multiple spleens, and absent or left-sided gallbladder

Malrotation

*Cardiac*

ASD or VSD

Partial anomalous pulmonary venous drainage

Pulmonary stenosis or atresia

Atrio-ventricular valve abnormalities

Absent coronary sinus

(Note moderate to low incidence of cardiac disease)

*Respiratory*

Bilobed lungs

Bilateral hyparterial bronchi

*Cardiovascular*

Dextrocardia

Right aortic arch

Azygos or hemiazygos continuation of the inferior vena cava

Absent hepatic segment of the inferior vena cava

*Also*

Female predominance No Howell-Jolly bodies in the peripheral blood (cf asplenia)

*From Rose et al (1975), Tonkin & Tonkin (1982) and Vaughan et al (1971).

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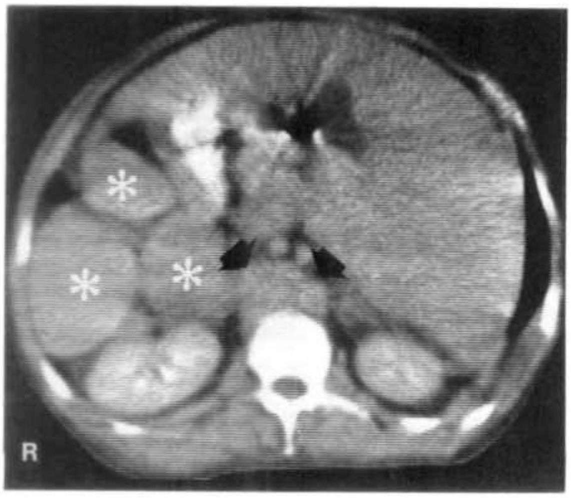

FIG. 1.

A CT scan of the abdomen shows multiple spleens (asterisks) and the liver on the left side. The irregular midline mass contiguous with the major vessels is lymphadenopathy (arrows).

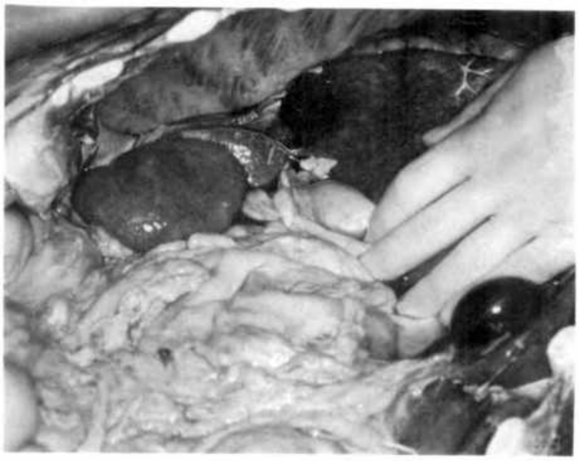

FIG. 2.

A post-mortem view from the patient's left side. The liver is beneath the pathologist's thumb and the gallbladder is underneath his little finger on the patient's left. Two spleens are visible on the far side, *i.e.* the patient's right, with the margin of a third spleen visible beyond.

condition remained undetected until the age of 42 years, when he developed Hodgkin's disease.

The aetiology of polysplenia is uncertain. Most cases are sporadic (Rose et al, 1975) but some familial cases, mostly with autosomal recessive inheritance, have been described (Arnold et al, 1983).

Radiologically, the features of polysplenia are well described (Table I). The abnormal visceral situs may be identified, in particular, by ultrasound or by CT scanning (Tonkin & Tonkin, 1982), or by radionuclide studies (Polga & Spencer, 1984), while gastrointestinal anomalies may be recognised on barium study (Paddock & Arensman, 1982). Changes related to the heart may be detectable on chest radiography (Vaughan et al, 1971; Rose et al, 1975) as well as by more specialised studies.

Thoracic isomerism may be recognised by the presence of bilateral hyparterial bronchi on frontal chest radiographs, where both bronchi are of equal length and both bear a similar relationship to the pulmonary artery (Soto et al, 1978). On the lateral view in polysplenia, both bronchi may be seen inferior and anterior to the corresponding pulmonary arteries, *i.e.* left isomerism. (Both bronchi lie posterior to the respective pulmonary artery in right isomerism.)

Among vascular anomalies, interruption of the inferior vena cava may be detected by ultrasound (Garris et al, 1980), CT (Tonkin & Tonkin, 1982) or angiography (Roguin et al, 1984). Anomalous venous return may be identifiable on chest radiographs: prominent azygos vein mimicking a right-sided aorta (Vaughan et al, 1971), for example, while hemiazygos return may be seen as a paraspinal mass (Floyd & Nelson, 1976) or as an aortic double density (Haswell & Berrigan, 1976). An absent vena caval shadow on the lateral chest radiograph is not a reliable indicator of the condition (O'Reilly & Grollmann, 1975). On CT, the enlarged azygos may be mistaken for retrocrural lymph nodes (Ginaldi et al, 1980).

Although lymphoma has been reported as a complication of ectopic or "wandering" spleen (Waldman & Suissa, 1978), a case of polysplenia with Hodgkin's disease has not, to our knowledge, been reported.

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# Early radiation swelling remains a problem in the management of paediatric brain tumours

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*(Received December 1986 and in revised form February 1987)*

Deteriorating neurological signs following the first fractions of radiotherapy for central nervous system tumours have long been recognised and categorised as "early radiation swelling" /oedema (Rubin & Casaret, 1968; Young et al, 1974), perhaps of vascular origin, comparable with primary radiation erythema of skin. However, with dexamethasone therapy and the relatively low daily fractional doses prescribed for paediatric brain tumours, it is nowadays uncommon to commence treatment with very low dose fractions, as precautionarily practised in the past. Indeed, several authorities (Kramer, 1968; Sheline, 1980) argue that such practice is unnecessary. We describe two cases that argue for individual assessment.

## CASE REPORTS

### *Case 1*

An 18-year-old man presented in July 1983 with headaches and vomiting There were minimal focal neurological signs There was no relevant medical history. Computed tomography (CT) demonstrated moderate hydrocephalus with no other lesion. The diagnosis of communicating hydrocephalus was made and a ventriculoperitoneal shunt inserted. Four months later he presented again with vomiting, headaches, unsteadiness of gait, diplopia and dysphagia Physical examination disclosed bulbar palsies and cerebellar signs, but apart from blurring of medial disc margins documented by one observer, there was no fundoscopic evidence of papilloedema During investigation severe bulbar dysphagia and respiratory problems were manifest A CT scan showed the shunt *in situ* and the lateral ventricles to be of normal size. The fourth ventricle could not be identified and a hypodense area that failed to enhance with contrast occupied the pons and extended to obliterate the fourth ventricle. Only the tip of the third ventricle could be identified, suggesting a tumour extending into it through the brainstem A vertebral angiogram and ventriculogram confirmed a mass extending from the tonsils of the cerebellum all the way rostrally to a mass occupying the third ventricle. Neurosurgical opinion was that biopsy would be dangerous and the clinical diagnosis of brainstem glioma made The patient was placed on 16 mg dexamethasone daily in divided dosage starting 7 days before radiotherapy. With the first radiation fraction (150 cGy, midplane delivered from opposed cobalt skull portals) the patient's neurological condition deteriorated rapidly at 4 h. His level of consciousness fell, tachypnoea with reduced respiratory effort occurred and the medical attendants thought the patient would die Mannitol was administered Twelve hours later his condition was much improved and radiotherapy continued in two 150 cGy fractions, rising to 175 cGy fractions. A total dose of 50 Gy was delivered. The patient made an excellent response to treatment. After 1 year, when he was not receiving any treatment, he obtained a place at polytechnic to study engineering Relapse occurred at the primary site at 18 months and death occurred at 2 years.

### *Case 2*

This 16-year-old boy presented with a short history of severe headache and vomiting. There were episodes of jerking of his right limbs There was no past history of note. Examination disclosed gross bilateral papilloedema and a mild left hemiparesis A CT scan showed an area of ring enhancement deep in the left cerebral hemisphere with extensive surrounding oedema occupying most of that hemisphere and with minor midline shift. The ventricles were compressed and hardly visible A burr-hole biopsy disclosed a low-grade glioma. Dexamethasone 16 mg a day was continued and the patient was referred to this unit for radiotherapy The radiation portals (lateral MV photon portals) encompassed most of the brain and a first fraction of 167 cGy was prescribed. Following this treatment and after a latency of 4 h the patient's condition markedly deteriorated His legs "gave way" and he fell when trying to walk He complained of severe frontal headaches and sleepiness, vomited three times and was cerebrally obtunded on examination. The pulse fell from 100/min to 60/min and blood pressure rose from 130/80 mmHg to 150/90 mmHg. Mannitol was administered and 12 h later the general condition improved to that before treatment. Radiotherapy continued with 100 cGy and thereafter 124 cGy followed by 150 cGy fractions without further incident.

## DISCUSSION

In the 5-year period 1982–86, 27 children have received radical radiotherapy for brain tumours in this department. Two developed complications that we ascribe to early radiation-induced swelling and these case histories have been described in detail.

In conclusion, where there is evidence of considerably raised intracranial pressure due to a large or a critically situated brain tumour, it would seem advisable to commence radiotherapy with low daily dose fractions (100–150 cGy), despite high-dose dexamethasone. A volume/field-size effect may also be important. Case 1 illustrates that a shunt will not necessarily circumvent this problem. Case 2 illustrates that this problem also occurs with extensive supratentorial tumours. The relatively low first fraction size in both cases as compared with previous data on early radiation oedema (Young et al 1974), is particularly noteworthy

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1987, *The British Journal of Radiology*, 60, 933–934

# Case of the month

## An unusual cause of gastrointestinal haemorrhage

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(*Received October 1986*)

An 18-year-old girl was referred for angiography of a lump under her right heel (Figs 1–3) which was painful on weight-bearing and limited her choice of footwear. On examination, four similar lesions were found elsewhere. She had had four substantial gastrointestinal bleeds requiring transfusion, as well as laparotomies for persistent gastrointestinal blood loss and suspected intussusception at which 27 bowel lesions were resected. See also Fig. 4. What is the diagnosis?

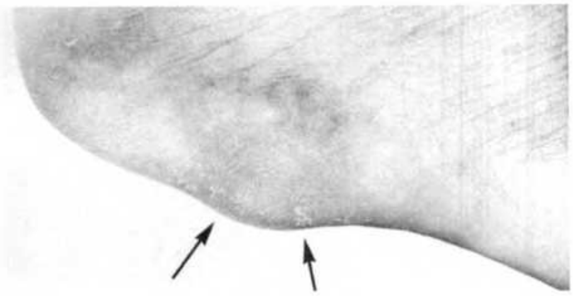

FIG. 1.

Lesion on right heel (arrows).

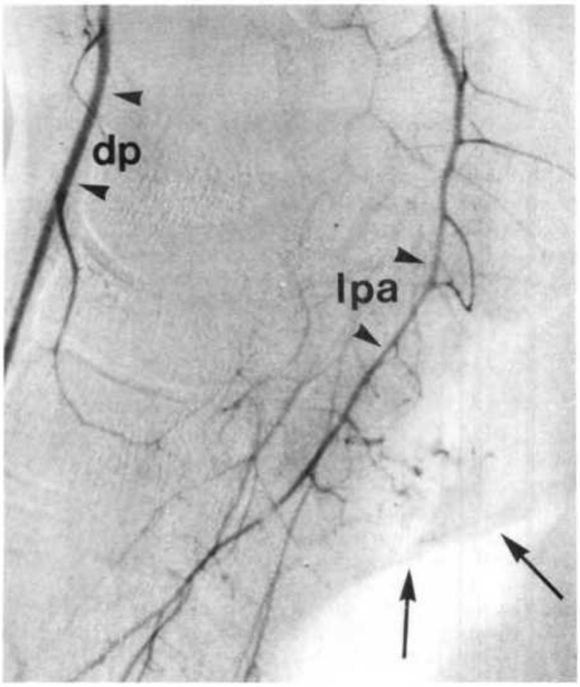

FIG. 2.

Lateral radiograph of right foot in external rotation. Arterial phase subtraction. (lpa = lateral plantar artery, dp = dorsalis pedis.)

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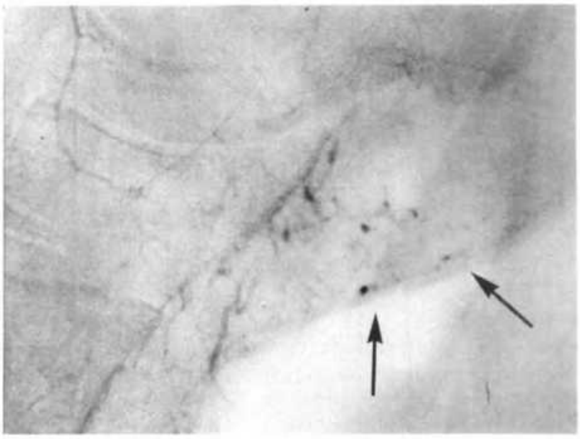

FIG. 3.

Venous phase subtraction.

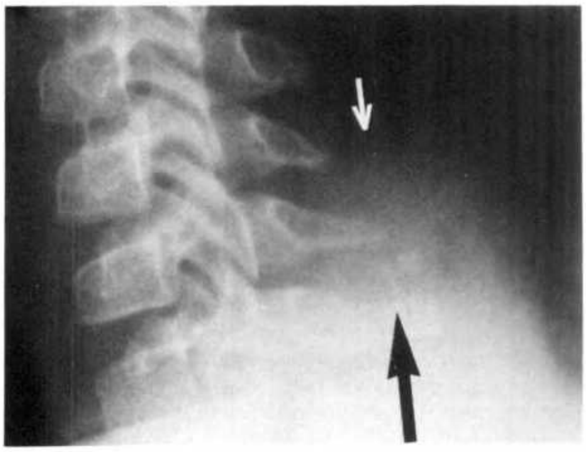

FIG. 4.

Lateral cervical spine at age 12 years (arrows indicate abnormality).

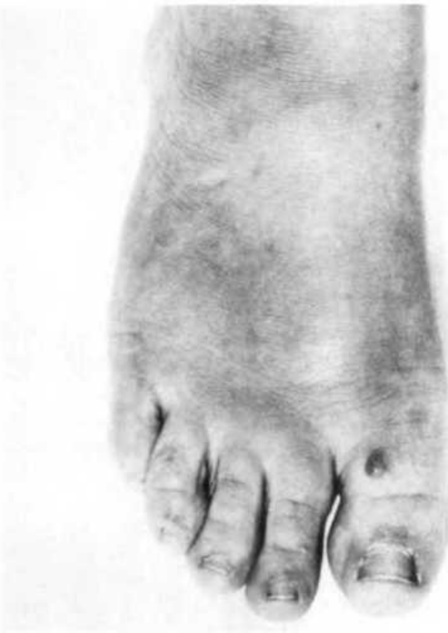

FIG. 5.
Blue rubber nipple on right great toe.

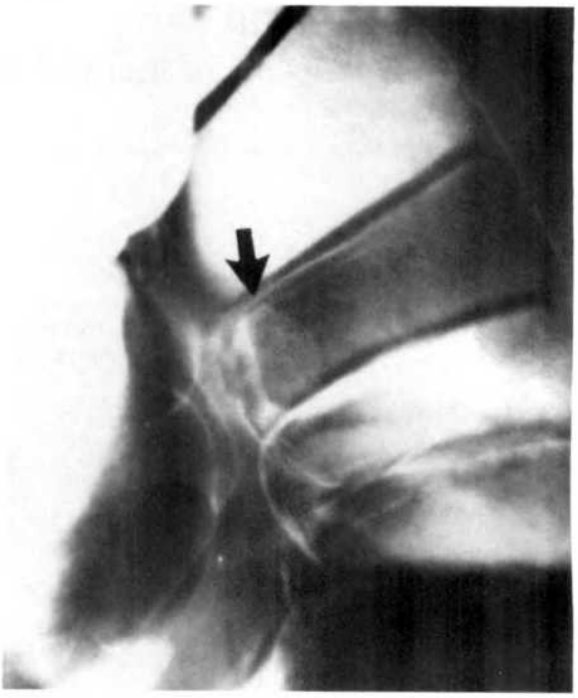

FIG. 6.
Double-contrast barium enema, performed 1 year after second laparotomy, showing a polyp (arrow) in the sigmoid colon.

The diagnosis is blue rubber bleb naevus syndrome (BRBNS).

In his original description, Bean (1958) described three characteristic skin lesions: Type 1, large disfiguring haemangiomas (Fig. 1); Type 2, blue rubber nipples that are compressible (Fig. 5); and Type 3, irregular blue-black macules. The lesions may be painful and associated with local hyperhidrosis. Lesions of the skin and bowel may be present at birth or develop on normal skin, and vary in number from one to several hundreds. Histologically, they are all cavernous haemangiomas.

Patients usually present for cosmetic reasons and/or gastrointestinal blood loss. The haemangiomas can occur throughout the gastrointestinal tract from mouth to anus but are more common in the small bowel. In association with BRBNS, cavernous haemangiomas have been described in virtually every organ and coelomic cavity (Rice & Fischer, 1962). The lesions are not pre-malignant but isolated cases of associated malignancies have been reported (Hoffman et al, 1978).

Radiology can assist the diagnosis by demonstrating phleboliths (Fig. 4), polyps on barium studies (Fig. 6) and the characteristic angiographic appearance (Figs 2,3) of a cavernous haemangioma, *i.e.* early opacification which then increases in the venous phase.

Angiography and radionuclide studies may help to localise gut lesions which are actively bleeding.

Recently, carbon dioxide laser therapy has been used successfully to remove the cutaneous manifestations (Olsen et al, 1979) and, with the development of endoscopic laser techniques, the need for multiple laparotomies may be obviated.

Blue rubber bleb naevus syndrome is an example of a rare dysembryoplasia; an autosomal dominant inheritance has been reported (Munkrad, 1983) but most cases are sporadic. It is included in the differential diagnosis of gastrointestinal polyposis syndromes with skin manifestations, namely Peutz–Jeghers, Osler Weber Rendu, Gardner's, Kaposi's, Cronkhite–Canada and Cowden's syndromes.

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1987, *The British Journal of Radiology*, *60*, 935–936 SEPTEMBER 1987

# Short communication

## Pituitary size in hypothyroidism as determined by computed tomography

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(*Received February 1987*)

Pituitary enlargement in association with primary hypothyroidism was first recognised by Niepce (1851), who found that in some cases of cretinism the pituitary gland bulged from its fossa. More recently, *in-vivo* evidence of pituitary-gland enlargement has been obtained using pneumoencephalography (Jawadi et al, 1978) and tomography of the sella turcica (Yamada et al, 1976; Bigos et al, 1978) but sellar enlargement has correlated poorly with the degree of biochemical hypothyroidism Bigos et al (1978) found that only those individuals with marked hypothyroidism had significant enlargement, while subclinically and moderately hypothyroid subjects did not differ from controls.

In recent years, attention has been drawn to the syndrome of primary hypothyroidism, hyperprolactinaemia and pituitary enlargement (Semple et al, 1983, Heyburn et al, 1986) and the question arises as to whether this is an uncommon syndrome or whether pituitary enlargement with or without hyperprolactinaemia is a common accompaniment of primary hypothyroidism.

On computed tomography (CT), there have been only isolated reports of pituitary enlargement in primary hypothyroidism (Pita et al, 1979; Silver et al, 1981). However, Katevuo et al (1985) have reported that CT, following administration of contrast medium, showed an increase in pituitary density in overt disease which was proportional to the serum level of thyroid-stimulating hormone (TSH), but they were unable to measure density in their subclinical subjects, neither did they measure gland height

We investigated pituitary gland size using CT in 23 patients with varying degrees of primary hypothyroidism.

### PATIENTS AND METHODS

Twenty-three individuals (age range 30–69 years; two men, 21 women) with untreated primary hypothyroidism (TSH > 6 0 mIU/l) were studied, with their informed consent. Ten had a normal serum $T_4$ level (54–142 nmol/l) and these were considered to be subclinically hypothyroid. One subject developed hypothyroidism subsequent to the administration of radioiodine for thyrotoxicosis. The remainder had autoimmune thyroiditis Serum $T_4$, TSH and prolactin levels were measured by Corning RIA kits

Eleven patients (age range 30–77 years; one man, 10 women) without evidence of endocrine disease, receiving scans for other clinical reasons, constituted the control group.

Scans were performed on a GE CT/T8800 scanner with a matrix of 320 × 320 All measurements were made with the same window width (300 HU) and level (70 HU) directly from the console unit. Patients lay in the prone position with the neck fully extended A lateral scan projection radiograph was used for localisation. Sodium iothalamate (100 ml, 420 mg iodine/ml) was rapidly injected intravenously and direct coronal scans perpendicular to the pituitary fossa floor were performed in contiguous 5 mm sections. The total scanning time was 11 s The height of the pituitary gland was taken as an index of its size Five patients with increased pituitary-gland height consented to be rescanned after at least 4 months of thyroxine replacement therapy when the TSH levels had returned to normal.

### RESULTS

In the control subjects the mean gland height was 2 9 ± 0.4 mm (mean ± SEM). The results for the study group are given in Table I Pituitary-gland heights in the subclinically (6.7 ± 0.6 mm) and overtly (5.6 ± 0 7 mm) hypothyroid groups (mean ± SEM) differed significantly from the controls ($p < 0.0025$ and $p < 0.005$ respectively) There was no significant difference between the subclinically and overtly hypothyroid groups ($p > 0.1$). Serum prolactin levels, measured in 15 patients (eight subclinically and seven overtly hypothyroid) were normal in 12 and marginally elevated in the remainder (one subclinically and two overtly hypothyroid)

Table II shows the reduction in pituitary-gland height in four subjects after treatment The fifth subject's pituitary gland appeared smaller but accurate measurement was not possible because of artefact

### DISCUSSION

Our results demonstrate that the pituitary gland is commonly enlarged in primary hypothyroidism and that this enlargement is as frequent in individuals with subclinical hypothyroidism as in those with overt disease. None of our subjects had a markedly raised prolactin level and this emphasises that lactotroph hyperplasia is not usually responsible for the pituitary enlargement This enlargement is reversible as the five individuals with overt hypothyroidism, who were rescanned after adequate replacement therapy, showed a decrease in pituitary-gland height although in one case this could not be accurately measured

Katevuo et al (1985) conducted CT scanning in 12 patients with hypothyroidism, of whom two appeared to have subclinical disease. Eight patients were shown to have increased density of the pituitary gland, but for technical reasons information could not be obtained in the two individuals with subclinical hypothyroidism These workers did not measure gland size Our findings indicate that, in addition to any increase in pituitary density in hypothyroidism, there is variable enlargement of the pituitary gland which is not directly related to the degree of thyroid dysfunction

Hyperprolactinaemia is a recognised accompaniment to primary hypothyroidism (Edwards et al, 1971, Semple et al, 1983) but none of our subjects had a markedly raised prolactin level Thus, it would seem that in primary hypothyroidism

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TABLE I

PITUITARY-GLAND HEIGHT AND THYROID FUNCTION OF PATIENTS SHOWN IN DESCENDING ORDER OF GLAND SIZE

| Case No | Age (years) | Sex | Thyroxine nmol/l (normal 54–142 nmol/l) | TSH mIU/l (normal <6 mIU/l) | Prolactin mIU/l (normal <400 mIu/l) | Vertical gland height (mm) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Overtly hypothyroid | Subclinically hypothyroid |
| 1 | 49 | F | <30 | >60 | – | 10 | – |
| 2 | 52 | F | 38 | >60 | – | 9 | – |
| 3 | 45 | F | 108 | 22.9 | 296 | – | 9 |
| 4 | 38 | F | <30 | 41.0 | 223 | 9 | – |
| 5 | 41 | F | 32 | 58.7 | – | 8 | – |
| 6 | 53 | F | <30 | >60 | 598 | 7.5 | – |
| 7 | 45 | F | 87 | >60 | – | – | 7.5 |
| 8 | 59 | F | <30 | >60 | – | 7.5 | – |
| 9 | 30 | F | 75–94 | 6.5–18.1 | 524 | – | 7 |
| 10 | 53 | F | <30 | 41.4 | 310 | 7 | – |
| 11 | 38 | F | 71* | 7.7 | 168 | – | 7 |
| 12 | 69 | F | <30 | >60 | 612 | 6.5 | – |
| 13 | 45 | F | <30 | >60 | 131 | 6.5 | – |
| 14 | 62 | M | 39–58*† | 4.2–7.2 | 100 | – | 6 |
| 15 | 51 | F | 45 | 27.2 | – | 5.5 | – |
| 16 | 50 | F | 65 | 30.0 | 184 | – | 5 |
| 17 | 54 | F | 76 | 9.5 | 277 | – | 5 |
| 18 | 55 | F | 32 | 39.6 | 199 | 5 | – |
| 19 | 62 | F | 96 | 20.7 | 216 | – | 4 |
| 20 | 66 | M | 41 | 48.0 | – | 3 | – |
| 21 | 44 | F | 81 | 20.2 | 334 | – | 3 |
| 22 | 38 | F | 32 | 47.0 | 188 | 2.5 | – |
| 23 | 52 | F | 70 | 13.7 | – | – | 2 |

*Brisk response to 200 $\mu$g intravenous thyrotrophin-releasing hormone (peak-to-basal ratio > 5).
†Thyroxine-binding globulin 9.2 mg/l (normal 8–23 mg/l). Level of free $T_4$ was normal.

TABLE II

CHANGE IN PITUITARY-GLAND HEIGHT FOLLOWING THYROXINE REPLACEMENT THERAPY

| Case No. | Height of gland before replacement (mm) | Height after replacement (mm) |
|---|---|---|
| 1 | 10 | 6 |
| 2 | 9 | 3 |
| 6 | 7.5 | 4 |
| 8 | 7.5 | –(artefact) |
| 12 | 6.5 | 3 |

pituitary-gland size does not correlate with circulating prolactin levels.

We have, therefore, shown that pituitary-gland enlargement is common in hypothyroidism and not invariably associated with florid disease.

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1987, *The British Journal of Radiology*, 60, 937–938 SEPTEMBER 1987

# Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

## Radiological interest in mammographic screening

THE EDITOR—SIR,

A nationwide mammographic screening service for breast cancer is to be introduced in the hope that community hospitals can reproduce the results achieved in some specialist centres. The service must be staffed by interested, enthusiastic and high-quality radiologists if cancers are not to be missed and inappropriate biopsies recommended. It is proposed that 120 screening units be established over the next 3 years, but the Forrest Report expresses concern that there may be difficulty in attracting suitable staff to this narrow field of practice. Some consultants may be prepared to give up some of their current workload to undertake mammographic screening but new consultant appointees will be expected to fulfil most of the screening commitment. A large proportion of the current pool of 255 senior registrars will need to develop an interest in mammography and therefore the results of the following straw poll may be of interest.

Seventy-seven senior registrars in the teaching centres of Bristol, Oxford, Kings College, Sheffield, Manchester, Edinburgh and Birmingham were asked three questions and 60 replied (78% response) as follows.

| | No | Yes |
|---|---|---|
| 1 Would you consider applying for a consultant post with a major interest in mammography? | 40 (66%) | 20 (33%) |
| 2 If a post were advertised with several sessions devoted to mammography would you regard this as a detraction? | 32 (54%) | 27 (46%) |
| 3 Do you feel confident in your ability to report mammograms? | 46 (78%) | 13 (22%) |

A surprising number of senior registrars may be prepared to devote much of their career to screening mammography but, paradoxically, few are confident in their ability to report mammograms. It is a fortunate coincidence that a willingness to try rather than confidence in the outcome is the very quality demanded by the Forrest proposals.

Yours, etc.,
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## Change in therapeutic gain with photon contamination in a neutron beam

THE EDITOR—SIR,

High linear energy transfer (LET) beams for radiotherapy are always contaminated with gamma rays. This will be a few per cent in a typical high-energy neutron beam (Fowler, 1981), increasing with depth in tissue as neutrons are captured (Maughan et al, 1981). For instance, for a typical high-energy cyclotron producing 8–22 MeV (mean energy) therapy neutrons at 10 cm depth or more, the gamma-ray component may exceed 20% (Fowler, 1981). This will decrease the biological effectiveness of the beam by decreasing the effective LET. In addition, there are fast protons which also are effectively low-LET particles.

Joiner et al (1984) determined the effect of increasing proportions of X-ray photons accompanying the neutrons (4MeV$_{d\rightarrow Be}$) on skin reactions in mice. In order to assess the change in therapeutic effectiveness with photon contamination, we have determined changes in tumour growth delay as a function of the proportion of the dose due to low-energy photons, using the same mixtures of photons and neutrons as Joiner et al (1984). In the present study the irradiations were given as single doses.

SaF tumours in CBA mice were transplanted and irradiated with X rays and neutrons as previously described (McNally et al, 1982). Tumour growth delay was assessed using standard methods (McNally et al, 1982) with six to eight tumours used per dose point. The neutrons were produced by accelerating 4 MeV deuterons onto a thick beryllium target to give neutrons with a broad spectrum and a mean energy of 2.26 MeV (Folkard, 1986).

The gamma-ray contamination with the neutron beam was 11% of the total dose. In order to irradiate tumours with different proportions of neutrons and photons, they were irradiated sequentially (without a gap in time of more than 1 min) giving neutrons and then photons. The proportion of the dose due to photons was 11% (neutron beam alone), 32%, 53%, 72% and 100% (X rays alone). For the group given 53% photons the order was also reversed, giving the photons first. The source of photons was a Pantak therapy X-ray machine operating at 240 kVp, 15 mA (half-value layer 1.3 mm Cu).

Joiner et al (1984) performed their experiments on skin, giving the neutrons and X rays simultaneously at dose rates of 0.22 Gy min$^{-1}$ and 0.20 Gy min$^{-1}$ respectively. These dose rates, especially for X rays, were too low to use for tumour irradiations, when there could be significant repair of radiation damage and, possibly, reoxygenation during the irradiation period. For this reason tumour doses were given sequentially at dose rates of 0.47 Gy min$^{-1}$ for neutrons and 4 Gy min$^{-1}$ for X rays. The order in which the radiations were given did not affect the tumour growth delay (see below) and, with cells *in vitro*, sequential and simultaneous irradiations gave the same result (McNally et al, 1985). Therefore, it would appear to be valid to compare the present tumour results with earlier skin studies (Joiner et al, 1984).

Figure 1 shows the tumour growth delay plotted as a function of total dose (neutrons plus photons) for the different mixtures of radiation. Neutrons, as expected, caused the greatest growth delay for a given dose and 100% X rays the least. The results for 53% photons show that essentially the same dose–effect curve was obtained whether the X rays or the neutrons were given first. A similar result was obtained for V79 cells *in vitro* (McNally et al, 1985).

In order to assess the therapeutic effect of changes in the proportion of the dose due to photons, tumour growth delay was plotted as a function of "skin reaction" for the different irradiation conditions. For a given skin reaction neutrons alone (plus 11% gamma rays) caused the most tumour growth delay and X rays the least. This probably reflects the presence

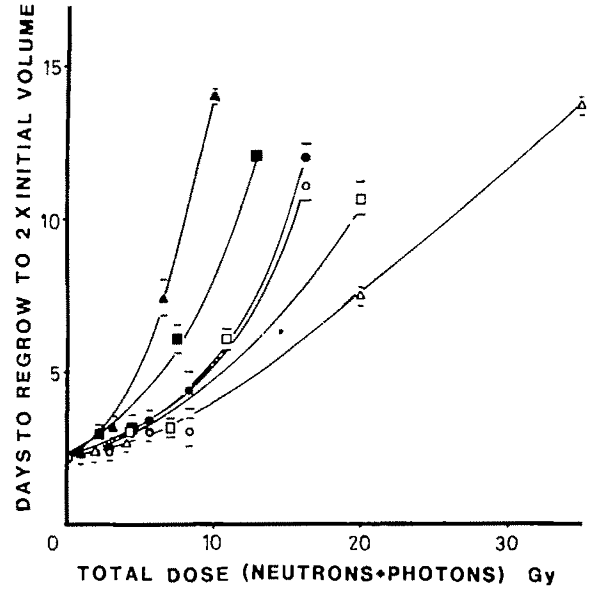

Fig 1.

Tumour growth delay versus total dose: ▲ neutron beam alone, ■ 32% photons, ○ 53% photons (N then X), ● 53% photons (X then N); □ 72% photons; △ X rays alone (error bars 1 SEM).

of a significant proportion of hypoxic cells in the tumour but not in the skin For the lowest skin reaction, if the photon contribution was ⩾32%, virtually the same growth delay was obtained For more severe skin reactions the line for 32% photons was between that for neutrons alone (plus 11% gamma rays) and the curves for 53% or more photons, all of which were close together (Fig. 2)

Measurements in water phantoms have shown that the photon component of the neutron beam may be as high as 53% at a depth of 20 cm in tissue (Maughan et al, 1981) This would greatly reduce the therapeutic benefit of this neutron beam, as is shown in Fig 2 For the much higher energy neutrons that are used clinically, the photon component of the total dose may only be between 7.8% and 28% at 20 cm depth (Fowler, 1981). From Fig. 2, for an average skin-reaction score of 1.5, a change in the photon component from 53% to 32% increased the tumour growth delay from 61% to 85% of the maximum delay, obtained with the neutron beam alone

Therefore, these results suggest that there may be a little loss of therapeutic benefit when tumours are treated at depth with clinical neutron beams when the low-LET component will be ⩽ 28% of the total dose For fractionated treatments, the influence of reoxygenation is likely to increase further the tumour response to low-LET radiation for a given skin reaction. Consequently there may be even less loss of benefit from low-LET contamination of high-LET beams with fractionation

Yours, etc.,

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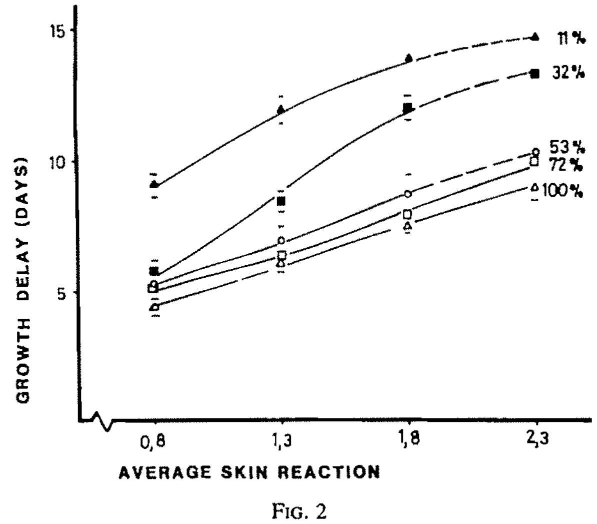

Fig. 2

Tumour growth delay versus average skin-reaction score (10–32 days) for different proportions of the dose due to photons. Symbols as for Fig. 1 Data points were obtained by using Fig 1 and the skin reaction versus dose data of Joiner et al (1984) The skin-reaction scale is that of Douglas and Fowler (1976).

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1987, *The British Journal of Radiology*, *60*, 939–940 SEPTEMBER 1987

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# Severe mental retardation in Japanese bomb survivors irradiated *in utero*: a postscript

THE EDITOR—SIR,

Recently, a variety of X chromosome-linked syndromes with severe mental retardation (SMR) has become recognised, the fragile X syndrome being, after Down's syndrome, the next commonest cause of SMR in a general population. It depends, like Down's syndrome, on an inherited anomaly and so will not be caused by irradiation after conception. Virtually all males with the fragile X chromosome are retarded but only a proportion, about one third, of females with the same chromosomal anomaly (Turner & Jacobs, 1983; Anonymous, 1986). Thus, an abnormally high ratio of males to females in bomb survivors with SMR after irradiation *in utero* might suggest further investigation to determine whether some cases attributed were in fact determined genetically. Families with more than one retarded son and mentally retarded males with enlarged testes show above-average frequencies of the fragile X chromosome (Primrose et al, 1986).

Severe mental retardation occurred without recorded significant clinical findings in four males and four females in nearly 1400 bomb survivors with fetal tissue dose in the range 0–9 cGy (mean about 1 cGy), *i.e.* controls (Table I). Males did not predominate and the overall rate is several times higher than the rate, about 1 in 1000, for SMR attributed to the fragile X syndrome in unirradiated Western populations (Anonymous, 1986). At fetal doses exceeding 1 Gy there were also equal numbers of males and females in those without significant clinical findings. However, of seven cases exposed *in utero* in the fetal dose range 10–99 cGy and classified as SMR without significant clinical findings, six were males and only one female (Table I).

Examination of these and the other cases for the fragile X chromosome (in blood lymphocytes cultured under specific conditions) or for associated but not invariable phenotypic features, such as enlarged testes (and overgrown ears and repetitive speech) (Turner & Jacobs, 1983), might allow cases to be reclassified as fragile X syndrome and thus not to be attributed to irradiation. Enlarged testes may also be found in other varieties of X-linked mental retardation. Since in bomb survivors exposed *in utero* there are so few cases of SMR without significant clinical findings on which to base a dose–response for induction of SMR by irradiation, and since the dose–response is so important for the practical purposes of radiological protection (Schull et al, 1986), a renewed effort to define aetiology in the light of recent discoveries might seem well worth while (cf. also Table I footnote). Consanguineous marriages, favouring the appearance of chromosomally linked defects in children, were commoner in Japan than in the West and in bomb survivors were differentially distributed according to dose (Schull et al, 1981).

TABLE I

NUMBER OF SUBJECTS WITH SMR AFTER *IN UTERO* EXPOSURE ACCORDING TO SEX, FETAL TISSUE DOSE, STAGE OF GESTATION AND PRESENCE OF CLINICAL FINDINGS*

| Fetal dose (cGy) | No. of cases of SMR | | Post-ovulatory age range (weeks) | No. of subjects at risk at all gestational ages |
|---|---|---|---|---|
| | Male | Female | | |
| With SMR and without significant clinical findings | | | | |
| 0–9 | 4 | 4 | 8–36 | 1377 |
| 10–99 | 6 | 1 | 8–24 | 203 |
| 100+ | 3 | 2 | 8–15 | 19 |
| 100+ | — | 1 | 25 | |
| With SMR and significant clinical findings† | | | | |
| 0–131 | 3 | 6 | 1–36 | |

*Data from Otake and Schull (1983)

†Listed in Mole (1987) and including one male with a "retarded sibling" and zero dose.

TABLE II

MATERNAL EXPOSURE IN THE CASES OF SMR IN JAPANESE BOMB SURVIVORS IRRADIATED *IN UTERO**

| With significant clinical findings | | | Without significant clinical findings | |
|---|---|---|---|---|
| No | Details | Maternal kerma (cGy T65DR) | No | Maternal kerma (cGy T65DR) |
| 5 | Retarded sibling,<br>Down's syndrome,<br>birth trauma,<br>syphilis,<br>Japanese B encephalitis | 0–2 | 7 | 0–5 |
| 1 | Down's syndrome | 28 | 1 | 17 |
| 1 | Down's syndrome | 96 | 2 | 81, 87 |
| 1 | Neonatal jaundice | 180 | 5 | 190, 190, 200<br>240, 260 |
| 1 | Neurofibromatosis | 310 | 1 | 290 |
| 0 | | | 5 | 380, 380, 490<br>520, 550<br>(lethal range) |

*Data from Otake and Schull (1983)

For all cases, and for the remaining cases after excluding those with a medically acceptable cause for SMR other than irradiation (Table II), the frequency of SMR is linearly related to fetal tissue dose in those exposed at 8–15 weeks post-conception, the radiosensitive stage of forebrain development (Schull et al, 1986, Mole, 1987). However, stating radiation exposure in terms of fetal tissue dose (Table I) obscures the gross maternal exposure in many of the cases of SMR. The mothers of 11 of the 21 with SMR and without a clinical diagnosis were exposed either in the near-lethal range 190–290 cGy or in the lethal range 380 cGy and upwards (Table II). It must be an act of faith to assume that such damaging maternal exposures contributed nothing at all to the development of SMR and that, therefore, linearity can be used without qualification as the basis for extrapolation to exposures 100 times smaller. The forthcoming revision of bomb-survivor dosimetry may change doses but cannot alter the number of cases of SMR. On the other hand, allocation of a medically defined cause to one or more of the cases assumed at present to have been caused by irradiation could be important, especially if any of the six cases, five male and one female, with maternal kerma 17–240 cGy (fetal doses 6–81 cGy) and exposed at 8–15 weeks, were to be so reclassified.

Below-average brain weight and histological findings suggesting defective neuroblastic migration in fetal life have been recorded in the fragile X syndrome (Turner & Jacobs, 1983) and have also been suggested as characteristic of SMR after irradiation *in utero* (Schull et al, 1986).

1987, *The British Journal of Radiology*, 60, 940–941

I am pleased to acknowledge the help of Professor M. Bobrow, Guy's Hospital, London, and Professor H. J. Evans, Medical Research Council Clinical and Population Cytogenetics Unit, Edinburgh.

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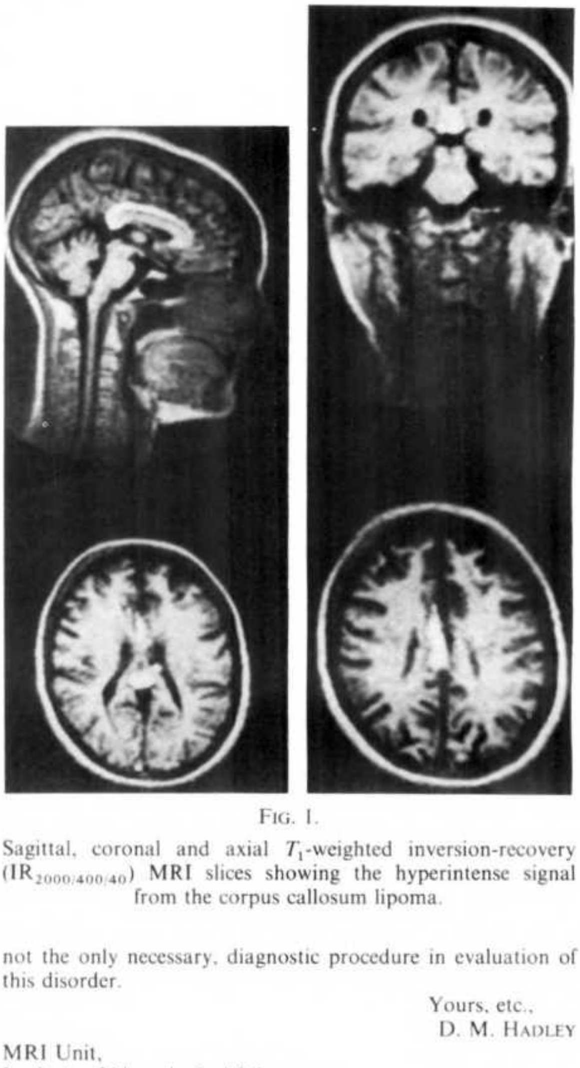

Fig. 1.

Sagittal, coronal and axial $T_1$-weighted inversion-recovery ($IR_{2000/400/40}$) MRI slices showing the hyperintense signal from the corpus callosum lipoma.

## Case of the month: lipoma of the corpus callosum

The Editor—Sir,

In Dr Hamilton-Wood's interesting discussion of the radiology of a corpus callosum lipoma he uses a rather dated reference (Harwood-Nash, 1977) to support the contention that computed tomography (CT) "is the most effective and least invasive tool in establishing the diagnosis of a lipoma of the corpus callosum". With the development of magnetic resonance imaging (MRI) this statement is now incorrect. Magnetic resonance imaging does not involve ionising radiation and can be performed in sagittal, coronal or axial planes without computer reformatting or uncomfortable patient positioning. A $T_1$-weighted spin-echo or inversion-recovery sequence clearly identifies the characteristic short $T_1$ signal from a lipoma (Fig. 1) in addition to delineating any associated midline anomaly (Curnes et al, 1986). The anterior cerebral and pericallosal arteries are shown by their "flow void" low signal and there is no necessity for intravenous contrast agents. Direct visualisation by MRI allows the detection of even minor structural abnormalities that might be quite subtle, or even indiscernible on CT (Davidson et al, 1985).

The lack of known biological injury at conventional field strengths and the ease of pluridirectional imaging without changes of patient position render MRI the indicated initial, if not the only necessary, diagnostic procedure in evaluation of this disorder.

Yours, etc.,
D. M. Hadley

MRI Unit,
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(*Received February 1987*)

(*Author's reply*)

The Editor—Sir,

I am grateful to Dr Hadley for his comments on this "Case of the month", and for his MRI illustrations. However, I do not think that because Dr Hadley is one of a fortunate minority of very-high-cost-technology users that the statement about CT is wrong. So far as I know, ionising radiation at diagnostic levels is not harmful; fat is easily identified on CT by its Hounsfield number, and no contrast medium was given in our patient. However elegant sagittal, coronal or multiplanar sections may be they make little difference to the diagnosis in most cases and it is idle to make claims that MRI is the only diagnostic procedure needed when the diagnosis was made on a plain radiograph. Perhaps when (and if?) the costs of MRI come down, its speed increases so that a reasonable number of patients can be scanned in a day, it has been around long enough for any potential dangers to have emerged, and the need to inject expensive components such as gadolinium has been evaluated, it may be possible to be as dogmatic as Dr Hadley

Yours, etc,
C. H WOOD

Department of Diagnostic Radiology,
Chinese University,
Hong Kong

(*Received April 1987*)

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# Proceedings of The British Institute of Radiology

## Practical aspects of magnetic resonance imaging

Abstracts of papers presented at the above joint meeting with The Royal College of Radiologists held at the Edward Lewis Lecture Theatre, Middlesex Hospital Medical School, London W1 on Wednesday, January 14, 1987

**Chairmen: Professor I. Isherwood and Professor B. S. Worthington**

Basic principles of magnetic resonance Imaging, by M. A. Smith
Magnetic resonance imaging strategies, by G. M Bydder
Practical aspects of magnetic resonance imaging, by B E. Kendall
Magnetic resonance imaging in spinal disease, by I Isherwood
Magnetic resonance imaging of the musculoskeletal system, by J. P R. Jenkins
The applications of magnetic resonance imaging in obstetrics and gynaecology, by B. S Worthington
The abdomen, by G. M Bydder
Magnetic resonance imaging flow, by J. J K Best

### BASIC PRINCIPLES OF MAGNETIC RESONANCE IMAGING

M. A. Smith

*Department of Radiological Sciences, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, Guy's Hospital, London*

The fundamentals of nuclear magnetic resonance (NMR) are briefly outlined, concentrating particularly on the aspects that are of particular relevance to radiology (Kean & Smith, 1986) The hydrogen nucleus—the proton—is used for magnetic resonance (MR) imaging because of its NMR sensitivity, coupled with its abundance in human tissue. The basic process of precession is described using the classical physics model, illustrating how the MR signal is produced by the rotating component of magnetisation which is perpendicular (*i e* transverse) to the constant magnetic field ($H_0$). A small group of protons was considered following a 90° RF pulse Magnetic interactions between the nuclei cause them to precess at slightly different frequencies, causing a loss of phase coherence which results in a gradual decrease in the net magnetic moment in the transverse plane In a perfectly uniform $H_0$ the time constant of this process is $T_2$ In practice, the $H_0$ field is not uniform, which speeds up the process ($T_2^*$) The time constant describing the return to the original equilibrium position is $T_1$ In all cases $T_1 \geqslant T_2 \gg T_2^*$ The saturation-recovery (or partial saturation), spin-echo and inversion-recovery pulse sequences were described The timing of these sequences influences the contrast of the image determining the contribution from the proton density, $T_1$ or $T_2$ in the tissue to the intensity of the image The $T_1$ and $T_2$ of tissue are mainly influenced by the ratio of free to bound water within the tissue (Mathur-de Vré, 1984) The basic components of an MR system are the main magnet, the magnetic gradient coils and the RF coil Commercial systems are available with the main fields between 0.02 T and 2.0 T The relative merits of low-, medium- and high-field systems are outlined The importance of choosing the most appropriate RF coil is illustrated and the advantage of surface coils, or closely coupled coils, in particular cases is shown

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### MAGNETIC RESONANCE IMAGING STRATEGIES

G. M. Bydder

*Royal Postgraduate Medical School, Hammersmith Hospital, London*

In X-ray computed tomography (CT), variation in signal intensity of an image can be explained in terms of a single image parameter, but at least 10 image parameters ($\rho$, $T_1$, $T_2$, $\delta$, flow, $\chi$, $T_{1\rho}$, diffusion, perfusion and RF absorption) are needed to explain all magnetic resonance images Pulse sequences are used to obtain images dependent on these parameters Image interpretation involves on the one hand thinking through conventional tissue properties in terms of these 10 parameters, and on the other hand relating these parameters to the observed signal intensity for different pulse sequences Much basic work remains to be done, but it is possible to interpret more images available at present on a fairly systematic basis using the first six of the image parameters listed above. This approach provides a wide range of choice for magnetic resonance (MR) imaging Advances in MR imaging can be related historically to the clinical application and exploitation of the basic image parameters. During the period 1980–82, image interpretation was accomplished using $\rho$, $T_1$, $T_2$ and during the period 1983–85 $\delta$, flow and $\chi$ were added. This is important in placing publications in their correct context For example, susceptibility effects due to organic iron in haemorrhage have only been understood and used since 1985. Their recognition has required work both in understanding the metabolism of organic iron compounds and the design of pulse sequences capable of detecting changes in susceptibility. Much more work remains to be done and developments exploiting diffusion, perfusion and $T_{1\rho}$ can reasonably be expected over the next 2 years

### PRACTICAL ASPECTS OF MAGNETIC RESONANCE IMAGING

Brian E. Kendall

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In the central nervous system magnetic resonance imaging (MRI) has significant advantages over computed tomography (CT) for the detection and determination of the extent and distribution of disease processes This is a consequence of the following

1 The sensitivity of the modality to small differences in the distribution of mobile protons and in disease-induced physical and biochemical changes which influence the relaxation coefficients. The $T_1$ and $T_2$ values are increased in those pathological processes which tend to incite either cytotoxic oedema (infarction, necrosis, intoxications), vasogenic oedema from disruption of the blood–brain barrier, or interstitial oedema from raised intraventricular pressure or ependymal disruption.
2 The facility of imaging in all planes. This is of particular importance in dealing with the longitudinally orientated brain stem and spinal cord and in clear demonstration of the relationships of pathological processes to adjacent nervous tissue.
3 The absence of bone-induced artefacts These are of particular significance in CT imaging adjacent to the skull base (pituitary, middle fossa), posterior fossa, including intracanalicular acoustic and jugular foramen tumours, foramen magnum region and the spinal cord. The use of air meatography for small acoustic neurinomas has been replaced by MRI. The demonstration of small brain stem and, especially, cord swelling used to involve computed myelography or cystography; MRI shows not only the swelling but often gives some indication of its nature The degree of distortion of the neuraxis induced by compressing lesions can be determined, and an estimate of the amount of damage caused to neural tissue can often be made
4 The lack of known biological hazard makes reasonable its application for detailed serial observation to elucidate the nature of a disease process or assess the effects of therapy.

The specificity of magnetic resonance is limited There are, however, important exceptions, including sensitivity to flow effects, which allow diagnosis of aneurysms, angiomatous malformations and blood-vessel occlusions The short $T_1$ of fat demonstrates congenital tumours (lipomas, dermoids, teratomas) and lipomeningocoele and other dysraphic states Paramagnetic substances include melanin and methohaemoglobin, which allow specific recognition of melanoma metastases and subacute and chronic haematomas respectively. Susceptibility effects reveal the presence of haemorrhage at an early stage and for prolonged periods during resorption For most other disorders, reliance must be placed on distribution, morphological characteristics and correlation with clinical and biochemical data, but even with such limitations MRI has revolutionised early diagnosis or conditions such as demyelination and certain degenerative disorders. Current limitations of MRI include lack of patient acceptibility of the imager (2–5%) and exclusion of certain patients with cardiac pacemakers and ferromagnetic aneurysm clips. Patient-monitoring devices may have to be modified, but, though more difficult, monitoring within the scanner can be achieved routinely Scanning time is currently long, making the method susceptible to movement artefact, but shorter scanning sequences are likely to become routine Any time-saving will reduce the high cost of the method. A further current disadvantage is the lack of a routinely available contrast agent, though this should be remedied in the near future A paramagnetic agent which penetrates the blood–brain barrier will be particularly useful for delineating the margins of pathological process from oedema and defining lesions, such as some meningiomas, which have similar signal intensities to the adjacent tissue Meningeal enhancement on X-ray CT is of diagnostic significance in granulomatous and neoplastic meningitis, which may not be shown on unenhanced magnetic resonance scans Lesions of cortical bone, including basal fractures, may not be evident, and small amounts of calcification, which may have some diagnostic significance in tuberous sclerosis, parasitic diseases and occasional tumours, may not be revealed by magnetic resonance Cerebrospinal-fluid leaks may be shown, but, currently, computed cisternography is the elective method of demonstration. Overall, MRI, as it becomes more widely available, will be the primary method of imaging the soft tissues of the central nervous system In a recent brief survey of our material, it provided more information than all other imaging methods in one third of cases and gave all the information provided by other methods in 20% Additional lesions to those shown on CT were present in 15%, and these were totally unsuspected in 10% The diagnosis made after CT was changed or substantially modified by MRI in 7.5%

## MAGNETIC RESONANCE IMAGING IN SPINAL DISEASE

I. Isherwood

*Department of Diagnostic Radiology, University of Manchester, Manchester*

Magnetic resonance imaging offers unique imaging access to the spinal canal and the neural structures within it. It also offers the facility to obtain a specific signal from the nucleus of the normal intervertebral disc Numerous options affecting slice selection, spatial resolution and contrast can be used to optimise image quality and examination time. Gadolinium DTPA, in certain circumstances, can improve sensitivity and reduce examination time Differentiation between intra- and extramedullary and extradural lesions is possible, while a variety of pathological processes, some hitherto inaccessible to imaging, can differ significantly in their signals Selection of imaging parameters to detect these differences can be critical Magnetic resonance imaging is of particular value in determining the extent of pathology and in the differentiation of cord and tumour cavitation, though caution is necessary in the normal-sized cord Magnetic resonance imaging appears to be as effective as myelography in the detection of disc herniation, particularly when used in conjunction with computed tomography A reduction in the signal intensity from the nucleus of the disc is a feature of intervertebral disc disease, though relaxation times are known to decrease with age. Spatial maps of $T_1$ and $T_2$ relaxation parameters can be used to reveal detailed structure and patterns of hydration Movements of water have been observed in the disc under stress and with varying posture. These factors need to be considered in quantitative studies.

## MAGNETIC RESONANCE IMAGING OF THE MUSCULOSKELETAL SYSTEM

J. P. R. Jenkins

*Department of Diagnostic Radiology, University of Manchester, Manchester*

Much interest has centred on the use of magnetic resonance imaging (MRI) in the assessment of the musculoskeletal system in both health and disease Where available, it is becoming the imaging method of choice in the evaluation of bone and soft-tissue tumours This is particularly so when reconstructive surgery, necessitating accurate pre-operative staging, is performed for limb salvage Magnetic resonance imaging (MRI) provides improved soft-tissue contrast and discrimination between tumour and normal tissue compared with computed tomography (CT) and, together with the multiplanar facility, the extent and margins of the mass can be more clearly delineated. In addition, the relationship of the tumour to the neurovascular bundle can be defined without the injection of contrast medium. In primary bone tumours involvement of cancellous and cortical bone, growth plate, joint space and adjacent soft tissue can be assessed Metallic prostheses and surgical clips degrade MR images to a much lesser degree than on CT scans, allowing assessment of tumour recurrence in the post-operative patient A limitation of MRI includes a poor demonstration of calcification, periosteal reaction and gas formation· CT remains the preferred imaging method for the detection of pulmonary metastases. In general, no distinction has been found between benign and malignant tumours in individual cases, and only a few tumour types (such as lipomas) can be specified Magnetic resonance imaging has been found to be an accurate method for the detection of early bone ischaemia of the femoral head. There is good delineation and separation of ligaments and cartilaginous structures with surface-coil imaging, allowing the complete assessment of joints in cases of trauma. Progress in MRI has been rapid over the last few years with the introduction of new pulse sequences, paramagnetic contrast agents, surface-coil imaging, oblique scanning facilities and improved data processing It can be seen, therefore, that more experience is required utilising these new advances before the true role of MRI in the musculoskeletal system can be defined.

## THE APPLICATIONS OF MAGNETIC RESONANCE IMAGING IN OBSTETRICS AND GYNAECOLOGY

B. S. Worthington

*Department of Radiology, University Hospital, Nottingham, United Kingdom*

Magnetic resonance imaging (MRI) promises to make important contributions to obstetric research and in clinical practice is a useful adjunct in those situations where ultrasound is limited The method allows one to perform pelvimetry without using ionising radiation. The placental site can be located with an accuracy comparable to ultrasound, but MRI is superior in defining the relationship of the lower margin of the placenta to the internal os. The distinctive appearance of the pregnant cervix offers the opportunity to study dystocia and incompetence and to examine the effect of ripening agents Measurement of the subcutaneous fat may allow assessment of the growth-retarded fetus Gestational trophoblastic neoplasia has a characteristic appearance and MRI may allow early detection of recurrent disease when high HCG titres are found Leiomyomas present a wide variety of appearances with MRI and their precise location and relationship to the endometrium and serosa can be seen Both ultrasound and computed tomography have limitations in the diagnosis of endometrial adenocarcinoma and Stage I and II carcinoma of the cervix Magnetic resonance imaging, however, can readily demonstrate the invasion of the myometrium and cervix in the former and show distortion of normal cervical anatomy and early parametrial involvement in the latter. Endometriotic deposits down to a few millimetres in size can be identified using heavily $T_2$-weighted spin sequences In ovarian masses, as well as providing excellent morphological detail, MRI can provide information regarding the contents of any cystic component More experience is needed to identify the patients who will benefit from MRI to the degree necessary to justify the high cost

## THE ABDOMEN

G. M. Bydder

*Royal Postgraduate Medical School, Hammersmith Hospital, London*

There are several reasons why magnetic resonance imaging (MRI) of the abdomen is technically more difficult than that of the brain (i) Respiratory and peristaltic movements are a far greater source of motion artefact than is the small pulsative movement of the brain (ii) The $T_2$ of liver is much shorter than that of brain, with the result that there is less time available to collect the data (iii) Fat is ubiquitous in the abdomen where it may be confused with long-$T_2$ lesions This is rarely a problem in the central nervous system (CNS). (iv) Bowel contents have variable properties whereas cerebrospinal fluid surrounding the brain has a uniform and relatively predictable composition. (v) The blood–brain barrier enhances the value of common intravenous contrast agents in the CNS; this is not true in the abdomen Various techniques have been used in order to compensate for some of these disadvantages These include the use of corset coils, respiratory ordered phase encoding (ROPE) to reduce artefact and the short TI inversion-recovery sequence which suppresses the signal from fat. More recently, fast $T_2$-dependent partial saturation sequences have been used to produce high-contrast images within breath-holding times Oral and intravenous magnetite may greatly increase the value of MRI in abdominal imaging, should they become available for human use.

## MAGNETIC RESONANCE IMAGING FLOW

J. J. K. Best

*Department of Radiology, Edinburgh Royal Infirmary, Edinburgh*

The reasons why flow, blood or other body fluids may affect the magnetic resonance experiment are discussed under the following headings

1 Signal intensity.
   (a) paradoxical enhancement,
   (b) spin washout,
   (c) phase cancellation,
   (d) even echo rephasing
2 Time of flight
3 Phase encoding
   (a) Fourier transform,
   (b) phase image.

Examples of flow effects in commonly used imaging pulse sequences are shown and possible pitfalls in clinical practice discussed A method for flow velocity measurement using phase encoding with even echo rephasing employing field echoes is discussed and clinical examples of cardiac and cerebrospinal-fluid flow shown.

*Proceedings of The British Institute of Radiology*

# Uroradiology update

Abstracts of papers presented at the above meeting, held jointly by The British Institute of Radiology, The Royal College of Radiologists and The Royal Society of Medicine (Section of Radiology), organised by The British Institute of Radiology and held at Institute House, 36 Portland Place, London W1N 4AT on Thursday, January 15, 1987

**Chairman: Dr D. Rickards**

Extracorporeal shock-wave lithotripsy at St Thomas' Hospital: a review of the first 1500 cases treated, by J. Pemberton
The use of transrectal ultrasound in the management of benign diseases of the prostate, by S. St. C. Carter
An overview of laser in urological practice, by G. M. Watson
Magnetic resonance imaging in carcinoma of the bladder, by R. J. Johnson
Scrotal ultrasound, by W. Lees (abstract not received)
Renal tract embolisation, by D. J. Allison

## EXTRACORPOREAL SHOCK-WAVE LITHOTRIPSY AT ST THOMAS' HOSPITAL: A REVIEW OF THE FIRST 1500 CASES TREATED

James Pemberton

*Department of Radiology, St Thomas' Hospital, London SE1 7EH*

The Dornier lithotripter was purchased by the British United Provident Association in 1984 and installed at St Thomas' Hospital, London, in March 1985, substantially for use within the National Health Service. Renal-stone disruption results from bombardment by shock waves generated from outside the body by an underwater, high-voltage condenser spark discharge of 1 μs duration. The condenser discharge explosively evaporates water and the resulting shock waves are focused by an ellipsoidal reflector. The target is the renal stone. Accurate positioning is made possible by means of a biplane image intensification system. The procedure involves the closest co-operation between the radiologist and the urologist. Initial assessment involves plain abdominal radiographs with tomography, an intravenous urogram and a baseline renal ultrasound. Auxiliary procedures were required in approximately 13% of patients These included percutaneous nephrostomy both for drainage and for placement of tubes for subsequent nephrolithotomy, ureteroscopy and, rarely, open operation. The procedure needed to be repeated in 7 8% of patients for complete disruption of their calculi. The average number of shocks per treatment was 1450 General anaesthesia was employed in 67% while the remaining 33% had epidural or spinal. A general anaesthetic was found to facilitate treatment. Fourteen patients became clinically septicaemic following the procedure and eight of these had positive blood cultures. There was one related death from septicaemic shock

## THE USE OF TRANSRECTAL ULTRASOUND IN THE MANAGEMENT OF BENIGN DISEASES OF THE PROSTATE

S. St. C. Carter

*Academic Unit of the Institute of Urology, London*

The recent resurgence of interest in transrectal ultrasonography (TRUS) for the diagnosis of early prostatic carcinoma has led to greatly improved imaging of the internal anatomy of the prostate. Little attention has previously been paid to the study of benign prostatic disorders. Prostatic ultrasonography in the patient with symptoms of obstructive micturition demonstrates the size and shape of the gland, which together with an estimate of the residual volume gives some information about the function of the outflow tract as well as the pathological nature of the obstruction Transrectal ultrasonography is of particular value in the assessment of patients whose symptoms persist or recur after transurethral resection of the prostate as residual obstructing prostatic tissue can be clearly identified.

Transrectal ultrasonography may also be used to investigate the patient with symptoms suggestive of prostatitis. Patients with established chronic infection as shown by a raised white cell count in the expressed prostatic secretion (EPS) have a variety of ultrasonic abnormalities including areas of echodensity in the peripheral and central gland and capsular irregularity and thickening Those cases with a normal EPS only exceptionally have changes on sonography, and might be classified as suffering from prostadynia. The ultrasonic signs of prostatitis can also often be seen in patients with haematospermia or secondary infertility. Congenital abnormalities and suspected obstruction of the ejaculatory apparatus may also be investigated by TRUS in patients with infertility or ejaculatory failure. Transrectal ultrasound of the prostate is of considerable value to the clinician in the management of a wide variety of benign conditions.

## AN OVERVIEW OF LASER IN UROLOGICAL PRACTICE

G. M. Watson

*Department of Urology, Middlesex Hospital and the St Peter's Hospitals, London*

A laser beam is a coherent, collimated and highly intense beam of light. Because of these qualities laser light can be passed at high energy through very fine quartz fibres The wavelength emitted is specific to the laser source; as the laser has an action only where it is absorbed, its action varies with that wavelength. Selecting a laser wavelength which is absorbed by a "target" tissue and not by surrounding tissue is the basis of the selectivity of action unique to lasers. Selectivity and miniaturisation are the main advantages that laser technology has to offer

Light from a carbon dioxide laser is absorbed at the immediate surface of a tissue and has a unique action of superficial vaporisation. However, it cannot be used under water or via conventional fibres and therefore has no value for more invasive procedures. Light from a neodymium YAG laser penetrates deeply through tissue, causing a homogeneous coagulation of tissue. It can be used via fine delivery fibres less than 1 mm in diameter. The limitation with coagulation of carcinoma of the bladder is the risk of unseen thermal injury to bowel It is therefore effective only for superficial tumours, but it can be used without general anaesthesia Laser coagulation of tumours of the upper tract may prove to be of much greater use It has been used for carcinoma of the prostate to treat the residual tissue after a second-look transurethral resection of the prostate This is because effective coagulation is limited to a depth of only 3 mm. It is therefore applicable only to early-stage disease.

Laser light is a convenient source for activation of haematoporphyrin derivative (HPD) for tumour therapy. Therapy is based on the prolonged presence of HPD in malignant tissue which has a cytotoxic effect when activated by light. There is therefore a selectivity of effect on tumour rather than normal tissue The difficulty with the technique is the provision of a homogeneous distribution of light in very irregularly shaped cavities This difficulty needs to be surmounted in order to avoid toxic effects on normal epithelium

A pulsed dye laser has been developed for fragmenting urinary calculi This has the advantages of selective absorption by the stone over the epithelium and of miniaturisation (the delivery fibre is 0 25 mm in diameter), making it less damaging to tissue than other modalities

The laser as a coagulator of tissue has to compete with diathermy in the lower urinary tract and thus far has not proved to have any advantage other than for superficial tumours as an outpatient manoeuvre where it is tolerated by the unanaesthetised patient better than electrodiathermy. It may prove useful in the upper tract. Selectivity of action is the main attraction of photoradiation therapy but it is difficult to put into practice. Miniaturisation and tissue sparing are particularly significant properties in the treatment of ureteric stones.

## MAGNETIC RESONANCE IMAGING IN CARCINOMA OF THE BLADDER

R. J. Johnson

*Department of Radiology, Christie Hospital, Manchester*

Important factors in the survival of patients with carcinoma of the bladder are the histological grade and stage of tumour at presentation The ability to identify the depth of tumour penetration into and through the bladder wall has important implications in treatment. The accuracy of computed tomography (CT) in staging carcinoma of the bladder ranges from 68% to 85% There are recognised limitations in identifying depth to tumour penetration and assessing the pelvic lymph nodes Local wall thickening is sometimes due to deep muscle invasion, enabling a distinction between T2 and T3 lesions to be made However, such an interpretation is unreliable as the bladder wall thickening may be due to muscle hypertrophy, the presence of oedema or a T2 lesion alone. Small intravesical lesions at the dome or base of the bladder can be missed on scans in the transverse axial plane. The value of CT is in delineating accurately extravesical extension of tumour beyond 0 5–1 cm, helping to identify inoperable patients and those who may be suited for radical cystectomy and for optimal radiotherapy planning.

Magnetic resonance imaging (MRI) has the potential to improve the accuracy of staging pelvic tumours The pelvic anatomy is well suited for study by MRI and the superior contrast resolution and multiplanar facility provide advantages over CT. Lesions at the dome and base are not missed and in studies comparing MRI with CT and surgery, MRI has proved a more accurate staging technique than CT However, MRI, like CT, cannot distinguish between mucosal, submucosal or superficial muscle invasion. There is debate as to whether distinction between early and late deep muscle involvement can be made In some respects the distinction between T2 and T3A lesions is artificial, as surgery is not able to identify the boundary between the superficial and deep muscle layers The important question is whether there is sufficient muscle preserved deep to the tumour to hold the wall together if an endoscopic resection is undertaken. This information would make some T3 lesions currently treated by radiotherapy amenable to endoscopic resection. Research in Manchester, using a 0.26 T superconductive magnet, has addressed this problem, particularly with a view to optimising imaging planes and pulse sequences to identify depth of tumour penetration into the bladder wall.

Our experience supports the published literature for the improved accuracy of staging This is mainly because of the greater ability to distinguish T3A from T3B lesions and to identify more readily enlarged nodes, as distinct from vascular structures At present an optimal pulse sequence, suitable for the majority of patients, to distinguish tumour, bladder wall and urine has not been identified A variety of spin-echo $T_2$-weighted sequences (time to repeat 1500–2000, time to echo 60–120) will provide a distinction between tumour and bladder wall but not enable identification of T3A lesions amenable to endoscopic resection. Work in progress continues using other pulse sequences.

## RENAL TRACT EMBOLISATION

D J. Allison

*Department of Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London*

Therapeutic embolisation is used in a variety of clinical circumstances for the management of renal and urinary tract problems It can be used to control acute bleeding in the kidney or bladder secondary to trauma, surgery, biopsy, tumour, vascular malformation, infection, vasculitis and other disorders The technique is particularly useful in patients in whom surgery would be difficult or dangerous, and in some instances obviates the need for a nephrectomy Superselective embolisation is usually possible and enables the technique to be used even in single kidneys or cases where renal function is severely compromised In benign vascular malformations affecting the renal tract, embolisation is usually the treatment of choice, as it is for such lesions elsewhere in the body

Embolisation can be used to help in tumour management in three ways: as definitive treatment for benign vascular tumours, as a pre-operative measure if a surgeon desires a vascular tumour to be rendered ischaemic prior to surgery; and as a palliative measure in cases of intractable bleeding from inoperable tumours. Embolisation of the pudendal vessels supplying the corpora cavernosa may relieve priapism in early cases, and can help to relieve pain even after the condition has been present for several hours or days The possible role of embolisation in the cure of impotence is currently being evaluated Cases of impotence due to incompetence of the valvular mechanisms in the deep penile veins may be corrected by occlusion of the incompetent venous channels with steel coils Thus, embolisation is an important interventional technique in the management of a wide range of vascular disorders affecting the renal tract and is replacing surgical treatment in several areas.

BIR Bulletin

September 1987

# Conversazione

This year's Conversazione was delightfully different. It began at Charing Cross, drifted down the Thames on board the pleasure cruiser the *Sydney Hull*, with fine weather and fine sherry, and docked at Greenwich. Doubtless, strings were pulled by our naval president, Roger Berry, and by Professor John Lakey, for the BIR to be given the freedom of the Royal Naval College.

To dine in the baroque glory of the Painted Hall, with a three-course meal and the College's best silver, was, I believe, regarded as a privilege by all the guests. After dinner, the 1987 BIR awards and the speeches were made in the plush lounge bar of the Queen Elizabeth Ante Room. The BIR also took this opportunity to confer Honorary Membership upon Lord Dainton, F.R.S., before the evening's scientific pursuits began. The chance to see "Jason", the experimental nuclear reactor in Professor Lakey's Department of Nuclear Science and Technology and to examine the equipment and displays presented by his staff, was surely a valuable and indeed a rare one—all the more so since the Department is housed in a Grade I listed building. For those not so inclined, there was a tour of the Chapel. The Chapel is remarkable: designed by Wren and Ripley in baroque style, it was subsequently redecorated in the age of rococo. For those who either could not choose between these enticing tours or who chose neither, the bar stayed open, although in fact the lounge soon emptied.

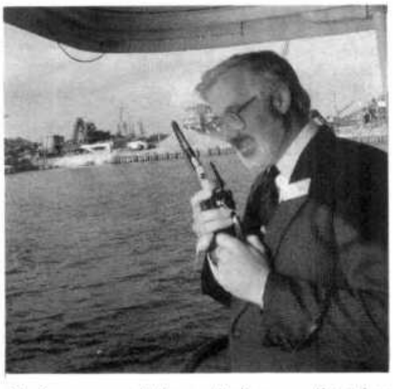
This year's Conversazione was heavily oversubscribed, with limited places both on the boat and at dinner, but those who were fortunate enough (perhaps astute enough!) to book early had an exceptionally enjoyable evening.

R. J. Footring

*The MV* Sydney Hull.

*BIR President Roger Berry and wife Val.*

*Left to right: new BIR honorary member Lord Dainton with Professor Berry and Admiral Milton-Thompson.*


*Professor John Lakey directing operations.*

*Professors E. Rhys Davies and B. S. Worthington deep in conversation.*

*Professor Lakey with BIR General Secretary Miss Susan Johnstone.*

# Obituaries

## Professor Philip Burch, M.A., Ph.D.

Professor Philip Burch, an outstanding radiation physicist and a pioneer in a modern theory of disease and ageing, died on March 22, after a short illness in his 67th year.

He came to Leeds University in 1949 where he remained throughout a constantly developing and successful career, highly regarded as a scientist and colleague with both national and international recognition. He was the holder of a personal chair in Medical Physics and had been deputy director of the Medical Research Council's Environmental Radiation Unit since its inception in 1959.

Born at Alconbury, Huntingdonshire, on April 15, 1920, Philip Robert James Burch was educated at Huntingdon Grammar School and was for a short time in the Post Office Engineering Department before serving in the Fleet Air Arm throughout the second world war. Thence to Cambridge where he graduated in natural science, with physiology included in Part I of the Tripos. Both this latter subject and his early practical experience of electrical circuitry were significant additions to his physics qualification and bore fruit in his later work.

Burch's research began with the measurement of the radioactivity of the body and resulted in the development of the first, and for a time the only, whole-body radiation monitor in this country, based on the use of high-pressure ionisation chambers and extensive water shielding. A further outcome of this research was a determination of the cosmic ray muon dose rate at sea level, a value that has remained in the literature, typified by the UNSCEAR reports, and supported rather than displaced by other later work. Burch made further important contributions in the field of whole-body radiation measurement when scintillators became available, in ionisation chamber theory, and in the variation of the radiation chemical yield with radiation quality. This and other research on the measurement of the environmental gamma radiation, and on theories of the action of radiation on cells, achieved a very high scientific recognition on their own account; indeed, they gained him the Roentgen Prize, and yet the most important part of Philip Burch's life's work was still to come.

In the early 1960s Burch became interested first in the induction of leukaemia by radiation, but soon in the causes of disease generally. Realising that the growth and homeostasis of normal tissues must be understood first, he took up Burwell's proposal that "in the mammal an essential function of lymphoid tissue is to establish and maintain morphostasis for many of its differentiated tissues" and worked with Burwell to develop and refine these ideas. Burch then began to devise a system of control for tissue growth—a "negative feedback" system in which efferent "mitotic control proteins" from a fixed number of stem cells (the central control element), were the effectors of tissue growth, balanced by afferent "tissue coding factors" from the target tissue. Initiation of disease then lay in a disturbance of this system. At the same time, he used well established mathematical methods to show that the age-specific incidence of many diseases could be accounted for by a small number of stochastic events. This opened up the use of a great deal of medical information and Burch collaborated with medical and dental colleagues in Leeds and elsewhere in this method of disease analysis—as many as two hundred diseases, from the autoimmune (autoaggressive, according to Burch) to cancer. These new ideas have not been universally popular, lending support, as they do, to inherited rather than environmental causes of disease, and sometimes making for lively controversy as in the case of smoking and cancer. But Burch's analyses and ideas are set out lucidly and comprehensively in his two books, *An Enquiry into Growth, Disease and Ageing* and *The Biology of Cancer, a New Approach*, and these show the depth of his research and the clarity and logic of his thought. The seminal ideas in these books must have a profound effect on future biological theory. His writings (more than 200 papers) brought him international recognition and many invitations to speak at conferences and in departments at home and overseas.

Philip Burch was always a delightful colleague, staunch in his friendship and, indeed, having friends throughout the University. His hobbies were music and art—he was a connoisseur of paintings and at one time chairman of the University Staff Art Society—and walking with his family in the Yorkshire Dales, which he loved. He leaves a wife, Dr Jane Burch, who has been his constant support, two sons and a daughter.

F. W. Spiers

## Bob Page 1910–1987

Friends and colleagues will be saddened to learn of the death of Bob Page on June 14, 1987 at the age of 77. Bob was for many years Kodak's Senior Sales Representative for the Central London and Teaching Hospitals before becoming National Sales Manager for the then-called Medical Sales Division, first at Kingsway and latterly at Hemel Hempstead.

Bob's career started in the Royal Navy and he joined Kodak Limited at the end of the Second World War. Through his excellent professional knowledge, his inexhaustible fund of stories and, above all, his inimitable capability of building up friendship, Bob was held in high esteem by a wide range of people in X-ray departments all over the country.

Bob retired in 1965 to Exmouth where he and his wife Jean continued to meet and entertain many friends. He is survived by his wife, his daughter Gill, son-in-law David, and their two children.

D. J. Nobbs

# Press releases

### New GE-Thomson deal

On July 24, 1987 Thomson SA of France and GE (USA), the American technology, services and manufacturing company, reached an agreement whereby Thomson will acquire GE's US-based consumer electronics business and GE will acquire Thomson-CGR SA, European-based medical equipment business.

Under the terms of the agreement, GE (USA) will acquire 80.1% of the shares of Thomson-CGR, a wholly owned affiliate of Thomson-CSF. A new European medical business holding company will be formed to combine the strengths of both GE and CGR in the design, production, and distribution of advanced technology medical diagnostic imaging equipment.

CGR will continue to manufacture and market medical equipment under the CGR name.

The transaction is subject to government reviews in the USA and Europe and is expected to be completed in 1987.

For more information tel. (31) 20-626011.

### Fetal ultrasound telemetry

Hewlett-Packard has introduced the HP 80240A fetal ultrasound telemetry system to provide accurate, non-invasive monitoring of patients, while permitting complete ambulatory freedom.

A wide-beam ultrasound Doppler transducer, together with the proven autocorrelation algorithm on the current HP 8040A or HP 8041A fetal monitors, allows accurate fetal heart rate (FHR) monitoring, even before the patient's membranes are ruptured. Uterine activity is monitored by an external tocodynamometer. This non-invasive approach to monitoring offers improved patient comfort and privacy.

An alternative to the external tocodynamometer is a hand-held event marker. This can be used by the mother to signal and record fetal movement, the onset of contractions or other significant episodes. The mother's only other contact with technology is a small telemetry transmitter that fits conveniently in a pocket or over a belt. Fetal and maternal data are transmitted to a remote telemetry receiver.

Further information is available from Ken Pett, General Manager, Medical Products Group (Tel. 0895-72020).

### 3M offer a complete ultrasound capability

The 3M Laser Imager system produces very high resolution images from many different input devices. A variety of image formats, 1, 4, 6 or 12 may be selected, with each pixel producing up to 256 shades of grey. Advanced laser optics enable production of images with no phosphor noise, optical distortion, monitor drift or edge "drop off". Developments are currently underway to enable several image acquisition modalities to be connected to the system via analogue or digital interfaces. Located in the central position of a radiography department the 3M Laser Imager can eventually become an imaging station, servicing up to six inputs simultaneously.

The Trimatic M Daylight Loading system is very suitable for the processing requirements of modern imaging modalities such as ultrasound. The ultrasound module incorporates a built-in XP 505 X-ray processor with high film throughput and utilises special 3M 10 in × 8 in CRT cassettes. Full microprocessor control of the system functions, with a self diagnostic programme, complete daylight film handling and a 15 s operating cycle, ensure high productivity and low service costs.

A new 3M Dry Silver medium-opaque film, is now available for monitor photography. It features an advanced Dry Silver emulsion on a polyester supporting base. The material is carbon backed for quick image processing by heat application. The image can be viewed easily without the use of a light box. The high D-max and increased contrast range of the new film provides an image background of high density with a gloss finish. The polyester base ensures good archival life and increases emulsion performance and stability. Taking the video signal from image acquisition equipment such as ultrasound, CT and image intensifiers, the 3M Dry Silver Imager can produce a dry, hard copy in just under 11 s.

Further information is available from Mr G. Smith, Marketing Executive, 3M Diagnostic Imaging Systems (Tel 0344-58458).

### 3M CRT film range extended for Siemens Multispot M camera

3M United Kingdom now market a new CRT film, designed specifically for use in the Siemens Multispot M camera. The characteristic curve of the film allows for wide exposure latitude, with optimum contrast for different applications. The fine grain emulsion ensures radiographic quality is enhanced, making the finest structures visible. The emulsion has been further enhanced to produce minimal RLF (reciprocity law failure), in the range of exposures used.

3M CRT film is available through the 3M national distribution network, or through the 3M Sales Office on 01-659-2323.

## DHSS X-ray equipment assessment reports

Information is once more available from the Department of Health and Social Security (DHSS) series of X-ray Equipment Assessment Reports. This comprises reports from the Kings Centre for Assessment of Radiological Equipment (KCARE) and the DHSS facility for measuring imaging performance at Leeds University, Department of Medical Physics (FAXIL). It also includes reports based on experience by National Health Service (NHS) staff, of different types of recently acquired equipment in their hospitals. These assessments are arranged by "Topic Group A" of the Radiological Sub-committee of the DHSS Radiological Advisory Committee. Although "Topic Group A" tries to ensure that its reports are free from gross error it should be remembered that each is primarily an expression of opinion by its authors and is not an official opinion; enquiries relating to the substance of "Topic Group A" reports are best directed to the hospitals concerned.

The DHSS considers that the following staff will need to have access to these reports and heads of departments should set up libraries for that purpose: diagnostic radiologists, consultant radiologists, superintendent radiographers, medical physicists, X-ray technologists and X-ray equipment supplies officers. Copies of the reports may be obtained free of charge by staff of the NHS and related authorities from: Report Distribution, DHSS, Supplies Technology Division, STD5, Room 312, 14 Russell Square, London WC1B 5EP. For organisations outside the NHS, copies are £25 unless otherwise indicated, and are available from DHSS Leaflets, PO Box 21, Stanmore, Middx HA7 1AY. (Overseas customers please add £4.00 if your payment is not made in sterling.)

A list of the assessment reports appeared in the *Bulletin* in July 1982. An up-to-date classified list follows overleaf.

### General

STB6A/84/19 Maintenance of radiological equipment in NHS establishments by equipment suppliers and other commercial agencies (£15)

STB6A/85/15 Acceptance inspections of radiological apparatus (proceedings of a DHSS seminar) (£10)

STB6E/86/5 Radiological society of North America Annual Conference (1985) (£10)

STD/87/6 Radiological Society of North America Annual Conference (1986) (£10)

### Miscellaneous equipment

STB/4/82 Johnson & Johnson Ltd: disposable examination gowns (KCARE report)

### Equipment accessories

STB/86/20 Assessment of Premise Engineering PREMAC mobile protective screen (KCARE report)

### Equipment QA test devices

STB6E/85/19 Evaluation of eight non-invasive electronic kV measuring instruments which are commercially available in the UK (FAXIL report)

### Cameras, film changers and imagers

STB/5/83 Comparison between 100 mm fluorography with Siemens system and full-size radiography (IF report)

STB6E/85/42 Introduction to imaging cameras with assessment of Matrix HPC 1010-4 (FAXIL report)

STB/86/21 Assessment of AFP/Matrix AM 1103 video pattern generator (FAXIL report)

STB/86/29 Physical evaluation of imaging performance of four different video imaging cameras (FAXIL report)

### Film handling/processing equipment

STB/4/76 Xeroradiography: summary of a questionnaire survey on the use of the Rank Xerox System 125 (£10)

STB/8/81 Applications of daylight film handling systems in the radiodiagnostic departments of NHS hospitals (£10) and Supplement No. 1 (1983) (£5)

STB/5/82 Kodak 'Automixer' for film processing chemicals (KCARE report)

STB/11/82 Kodak RP X-Omat film processor Model M6A-W (KCARE report)

STB/9/83 Agfa Gevaert R10 Gevamatic small format film processor (£10)

STB/11/83 Durr Med Medicine 260 small format film processor (£10)

STB/3/84 Kodak RP X-Omat film processor model M7B (KCARE Report)

STB/85/24 Kodak M8 radiographic film processor (KCARE report)

STB/86/23 Assessment of an MCP-Metelec Limited Metamatic fixer recycling/silver recovery unit (KCARE report)

### Digital imaging

STB/2/83 Digital radiology seminar

STB/18/83 Digital fluorography: guidance notes on technical specifications (£10)

STB6E/84/28 Clinical, operational and technical experiences with a digital vascular imaging system (FAXIL report)

STB6E/85/1 DSA test phantoms commercially available in the UK (FAXIL report)

STB6E/85/4 A procedure for evaluating the physical imaging performance of a digital subtraction fluorography system (FAXIL report)

STB/86/8 Assessment of an IDIS digital fluorography system (KCARE report)

STB/86/26 Application of digital subtraction angiography equipment in the NHS: the results of a questionnaire (FAXIL report)

STB/86/34 Assessment of Quantel IDIS digital subtraction angiography system—Bristol Royal Infirmary (£10)

### X-ray generators

STB/7/76 Picker Transix 800 X-ray generator (GEC Medical Equipment Ltd) (£10)

STB/5/77 GEC Summit 803 generator (£10)

STB/19/77 GEC Roentgen 703 generator (£10)

STB/8/80 X-ray installations with shared generators (£10)

STB/13/81 GEC Roentgen 863 generator (KCARE report)

STB/2/82 Siemens Tridoros 712-MP X-ray generator (KCARE report)

STB/4/84 Philips Maximus TM 100 X-ray generator (KCARE report)

STB/8/84 Picker International Vector 100 X-ray generator (with August 1984 supplement) (KCARE report)

STB6E/85/27 Siemens Polydoros 80 X-ray generator (KCARE report)

STB6E/85/28 Philips Medical Systems Saturn 500 and Saturn 850 X-ray generators (KCARE report) (£10)

### Antiscatter grids

STB/3/83 Comparative assessment of four secondary radiation grids (KCARE report)

STB6E/85/37 Antiscatter grids—Soyee Products—Korea (KCARE report)

### X-ray image intensifiers

(i) Image intensifier and closed-circuit TV systems

STB/2/80 The importance of some characteristics of TV monitors to the overall performance of image intensifier systems (IF report)

STB/10/81 Measurements of Siemens Sirecon 2 Videomed 3 and N systems (IF report)

STB/11/81 Vertec TV 762 image store (IF report)

STB/12/81 Leeds and KCARE assessment of GEC Kompact 9 HD Series 2 image intensifier systems (KCARE/IF reports)

STB/7/82 The testing of X-ray image intensifier television systems, 2nd edit., 1985 (report of a DHSS working group) (£10)

STB/14/83 Siemens Planicon panel-type X-ray image intensifier (FAXIL report)

STB/16/83 Siemens Videomed HR high resolution radiological television system with three types of modern X-ray image intensifiers (FAXIL report)

STB/5/84 Picker International Kompact S-80 TV fluoroscopy system with the modified VC 382 TV channel (FAXIL report)

(ii) Mobile image-intensifiers

STB/1/81 Wolverson MTH C-A mobile image intensifier X-ray unit (KCARE/IF reports)

STB6E/85/30 Siemens Siremobil 3N and 3H mobile image intensifiers (FAXIL report)

STB6E/85/33 Lixiscope hand held image intensifier with radioactive source (KCARE report)

### Injectors

STB/10/79 Cordis flow rate, Medrad 4, Angiomat 3000 and Simtrac angiographic contrast medium injectors (£10)

### Mammography

STB6E/86/1 Assessment of Wolverson X-ray (Acoma) MXR 102 mammographic unit (KCARE report)

STB6E/86/2 Assessment of Medical X-ray Supplies (Soredex) Mammex DC mammographic unit (KCARE report)

STB6E/86/3 Assessment of Elscint MAM LS-3 mammographic unit (KCARE report)

STB/86/27 Assessment of Philips Mammo Diagnost UM (KCARE report)

STD/87/7 Assessment of Xerox 120 mammography unit (£10)

### Mobiles and portables

STB/20/77 Philips mobile condenser discharge unit (£10)
STB/14/79 Todd motorised mobile capacitor discharge X-ray unit type TR Super (KCARE report)
STB6E/84/29 Siemens Mobilett Mobile (KCARE report)

### Bucky stands

STB/6/81 GEC Vertibucky single column bucky stand (KCARE report)

### X-ray tube supports

STB/7/81 GEC Apollo X-ray tube ceiling suspension with GEC Sectograph tomographic attachments (KCARE reports)

### X-ray tables

STB/6/78 Todd Research Lineargraph tomographic table (£10)
STB/8/78 GEC Linotome 40 linear tomographic table (£10)
STB/9/78 CGR Angioskelograph-6 (CGR Arteriophlebographe) (£10)
STB/5/81 Comparative assessment of five floating top radiographic tables (KCARE report)
STB/9/81 GEC Senate fluoroscopy table and GEC Sectograph 40 tomographic attachment (KCARE report)
STB/1/82 GEC Ensign variable height bucky table (KCARE report)
STB/6/82 Picker Rapido/Rap-X automated cassetteless radiographic system (£10)
STB/9/82 Philips BT-S4 bucky tomographic system (incorporates 1984 supplement) (KCARE report)
STB/17/83 Philips Bucky Diagnost general purpose bucky table (KCARE report)
STB/2/84 Penta XT radiography table (£10)
STB/7/84 Picker International Rapido 400 automated radiographic table (KCARE report)
STB6E/85/8 Assessment of Wolverson Mylo X myelography/tomography tables at two hospitals (£10)
STB6E/85/45 Assessment of Picker Modulex T for radiography tomography and occasional peripheral angiography (KCARE report)

### Examination systems

(i) Radiography
STB/12/82+83 addendum. Analytic Morphograph CF-1 (Kent Laboratory Services Ltd) (£10)
STB/8/83 Todd Research Triton Compact 500 generator with bucky table and floor to ceiling tube support (KCARE report)
STB6E/85/34 Siemens basic radiographic system to modified WHO specifications (KCARE report)
STB6E/85/36 Todd Research basic radiographic system to modified WHO specifications (KCARE report)
STB/86/16 Assessment of Philips Compact Diagnost 1 radiography system (KCARE report)
STB/86/24 Assessment of Siemens Palomex Zonarc unit (£10)
STD/87/1 Clinical evaluation of Siemens' Vertix B BRS stand and Polyphos 30R generator
(ii) Fluoroscopy/radiography
STB/6/79 GEC Concord 90/90 diagnostic table (with supplement) (£10)
STB/5/80 Three Philips Diagnost 73 tables, one with 73p paediatric accessories (£10)
STB/4/81 Wolverson Telematic 2 remote X-ray examination system (KCARE/IF reports)
STB/3/82 A basic Shimadzu fluoroscopy/radiography package (KCARE/IF reports)
STB/7/83 International General Electric fluoroscopy/radiography package RFX 90/MPX 80 (KCARE/FAXIL reports)
STB/13/83 Siemens Siregraph B table, Polyphos 500 generator, Sirecon 2–25 image intensifier and Videomed K (KCARE/FAXIL reports)
STB/15/83 IGE MSX 125 generator, Telegem 2 remote control table and 105 mm camera (£10)
STB/10/84 CGR Futuralix 1600 remote control X-ray table with Triplunix generator and associated equipment (£10)
STB6E/85/2 Philips Diagnost 88 remote control fluoroscopic/radiographic table with MCM80 generator (KCARE report)
STD/86/33 Assessment of Shimadzu conventional 90/90 radiographic fluoroscopic system with 100 kW generator and 12″ intensifier (KCARE/FAXIL report)
(iii) fluorography/special procedures
STB/11/79 Philips Polydiagnost C installation (£10)
STB/6/80 Siemens Infantoskop paediatric table (£10)
STB/12/83 Picker System 1200 for 100 mm fluorography (£10)
STB/86/28 Assessment of Picker International Senate 12 GW fluorography imaging system. Royal Victoria Infirmary, Newcastle (£10)
(iv) Thoracic
STB/6/84 Picker International Servochest System with a capacitor discharge generator (KCARE report)
STB6E/85/14 Picker International Clinix C chest radiography unit (KCARE report)
STB6E/86/4 Assessment of Siemens Optilux 57 intensifier associated with the Sircam 100 mm camera and Polyphos 300E generator (KCARE/FAXIL report) (£10)
(v) Cranial
STB/10/82 Philips Pendo Diagnost and Traumob C System for skull radiography (KCARE report)
(vi) Angiography
STB6E/85/45 Assessment of Picker Modulex T for radiography, tomography and occasional peripheral angiography (KCARE report)
STB/86/7 Assessment of IGE L/U ARM angiographic unit (£10)

### Films and screens

STB/3/81 Measurements on Du Pont film systems: characteristics of screen–film systems and their measurement; characteristics of rare earth screens (IF report)
STB/4/83 Measurements on Kodak screen–film systems (IF report)
STB/6/83 Comparative assessment of a range of 100 mm and 105 mm fluorographic film (FAXIL report)
STB6E/85/26 A physical evaluation of the imaging performance of the Agfa-Gevaert range of screen–film systems (FAXIL report)

### Gamma cameras and accessories

STB/11/80 Performance assessment of gamma cameras, Part 1
STB/13/82 Performance assessment of gamma cameras, Part 2
STB6D/85/6 Performance assessment of gamma cameras, Part 3
STB/86/9 Performance assessment of gamma cameras, Part 4

### Ultrasound—general

STB/86/6 American Institute of Ultrasound in Medicine Meeting (1985) (£10)
STD/87/8 Assessment of ultrasound scanners: Dynamic Imaging 'Concept', Irex 'Meridan', Siemens 'Sonoline SX', Diasonics 'DRF 200', Hitachi 'EUB 240'

### Computed tomography

STB/86/10 Comparison of the imaging performance of CT scanners (issue 4)

### Volumes of *BJR* for a good home

A complete set of *BJR* (unbound) 1962–85 is available for donation. Please contact the Editorial Office (01-580 4189) to arrange for collection.

# Library news

**The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)**

*The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085)*

*The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the* Bulletin*. Most books (excepting the historical collection) are available on loan.*

*There is an agreement which allows BIR members limited use of the RSM Library for reference purposes. Members should apply to the BIR Librarian for a visitor's card*

**Recent additions to the Library**

CEC. Occupational radiation dose statistics from light-water power reactors operating in Western Europe 1987
Del Regato, J. A.: Radiological physicists. 1985
Ginai, A. Z.. Contrast media for radiological examination in gastrointestinal tract leakage 1987*
Jacobs, C. (Ed.). Cancers of the head and neck. 1987
Kressel, H. Y. (Ed.). Magnetic resonance annual. 1986
McKenzie, A. L. et al (Eds). Radiation protection in radiotherapy. 1986
NCI Monograph 1986, 1: Adjuvant chemotherapy and endocrine therapy for breast cancer. Proceedings.
NCI Monograph 1986, 2. Cancer control objectives for the nation. 1985–2000.
NCI Monograph 1987, 3. Labeled and unlabeled antibody in cancer diagnosis and therapy Symposium.
NCRP Report No. 83 The experimental basis for absorbed dose calculations in medical uses of radionuclides 1985

*New periodicals*
Journal of medical imaging
Journal of thoracic imaging (on approval)

**Current journals held in the BIR Library**

Acta Oncologica
Acta Radiologica—Diagnosis
American Journal of Neuroradiology
American Journal of Roentgenology
Annales de Radiologie
Annals of the ICRP
Applied Health Physics, Abstracts and Notes
Applied Radiation and Isotopes
Astro Newsletter
Australasian Radiology
BMUS Bulletin
British Journal of Cancer
British Journal of Radiology
British Medical Bulletin
British Medical Journal
British Society of Dental and Maxillofacial Radiology Newsletter
BSI News
Cancer
Cancer Research
Cancer Research Campaign Annual Report
Cancer Treatment Reviews
Cardiovascular and Interventional Radiology
Cell and Tissue Kinetics
Chinese Journal of Nuclear Medicine
Chinese Journal of Radiology
Clinical Nuclear Medicine
Clinical Physics and Physiological Measurements
Clinical Radiology
Computerized Radiology
Critical Reviews in Diagnostic Imaging
Current Contents (Life Sciences)
Current Opinion in Cardiology
Current Opinion in Gastroenterology
Current Problems in Diagnostic Radiology
Deutsche Roentgengesellschaft Informationen
Diagnostic Imaging (USA)
European Journal of Cancer and Clinical Oncology
European Journal of Nuclear Medicine
European Journal of Radiology
European Journal of Surgical Oncology
Excerpta Medica 14 Radiology
Excerpta Medica. 23 Nuclear Medicine
Fortschritte auf dem Gebiete der Roentgenstrahlen
Gastrointestinal Radiology
Health Physics
HPA Bulletin
IAEA Newsbriefs
ISRRT Newsletter
International Agency for Research on Cancer. Annual Report
International Atomic Energy Agency Bulletin
International Journal of Hyperthermia
International Journal of Radiation Biology
International Journal of Radiation Oncology, Biology, Physics
Investigative Radiology
Japanese Journal of Nuclear Medicine
Journal Belge de Radiologie
Journal de Radiologie (France)
Journal Européen de Radiothérapie
Journal of Clinical Oncology
Journal of Clinical Ultrasound
Journal of Computer Assisted Tomography
Journal of Interventional Radiology
Journal of Medical Imaging
Journal of Nuclear Medicine
Journal of the Canadian Association of Radiologists
Journal of The National Cancer Institute
Journal of The Royal Society of Medicine
Journal of The Society for Radiological Protection
Journal of X-ray Technology
Lancet
Magnetic Resonance in Medicine
Medical Physics
Medical Radiography and Photography
Medicamundi
Meditsinskaya Radiologiya (USSR)
Meetings on Atomic Energy
Neuroradiology
Nuclear Medicine and Biology
Nuclear Medicine Communications
Oncologia (Rumania)
Pediatric Radiology
Physics in Medicine and Biology
Proceedings of The American Association for Cancer Research
Proceedings of the American Society of Clinical Oncology
Rad
Radiation Protection Dosimetry
Radiation Research
Radiatsionnaya Biologiya (USSR)
Radiographics
Radiography
Radiography News
Radiologia Medica (Italy)
Radiologic Clinics of North America
Radiological Protection Bulletin
Radiology
Radiology Now
Radiotherapy and Oncology
Rays
Seminars in Interventional Radiology
Seminars in Nuclear Medicine
Seminars in Roentgenology
Seminars in Ultrasound
Skeletal Radiology
Strahlentherapie und Onkologie
Ultrasonic Imaging
Ultrasonics
Ultrasound in Medicine and Biology
Urologic Radiology
World Health
Yearbook of Diagnostic Radiology

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*Free copies are available from Dr A. Z. Ginai, Department of Radiology, University Hospital, Dijkzigt, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands*

# BIR calendar events

*Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).*

*The meetings are at 36 Portland Place unless otherwise stated Attendance is open to non-members*

**Imaging in Dementia**
October 15, 1987 at 5 30 p m.
Organised by the Diagnostic Methods Committee.
Chairman. Dr P J. Ell.
Speakers. Prof. R Levy, Dr R. Wise, Dr P J. Ell, Dr N. Antoun and one other.

**Chemical Modification of Radiation Effects: Experimental and Clinical**
November 13, 1987 at 11 00 a.m.
All-day radiobiology work-in-progress meeting.

**New Radiopharmaceuticals and Their Clinical Applications**
November 27, 1987
Scientific Societies, London W1
Organised by the Nuclear Medicine Subcommittee.
Speakers. Dr F Brady, Dr I. Brown, Dr D Le Bars, Dr B. Langstrom, Dr M. C Lasne, Prof N A. Lassen, Dr H J. Machulla, Dr M. V Merrick, Dr A. D Nunn and Dr G. D Zanelli.

**Lasers—Applications in Radiology**
January 14, 1988 at 5 30 p m
Joint BIR/RCR/RSM meeting
Chairman Dr W D Jeans
Speakers Dr A L Mackenzie, Dr D C Cumberland, Dr S G. Bown, Mr D Rothery, Dr G Watson and Dr S Hart.

**Institute Sponsored Visits**

Members should write to the General Secretary of the BIR for application to either of the visits below

**Stockholm:** to the clinic of the late Dr Curt Westman, now owned by AB Medicinsk Roentgen

**Paris:** to radiotherapy centres in Paris, arranged through the collaboration of Professor M Tubiana

**Clinical Usefulness of Nuclear Medicine Image Processing**
February 9, 1988
Joint IPSM/BIR meeting organised by the IPSM
Further details: General Secretary, IPSM, 2 Low Ousegate, York YO1 1QU (Tel 0904-610 821)

**Functional Insights From Magnetic Resonance**
February 17, 1988
London, venue to be confirmed
Organised by the Diagnostic Methods Committee
Chairmen Prof. B S. Worthington and Dr G Bydder
Speakers Dr M. A Smith, Mr D. Longmore, Prof. P Mansfield, Dr I Young, Dr Hadley, Prof. I. Isherwood, Dr S Williams, Dr Edwards, Dr B. Ross, Prof. O Reynolds, Dr J Cox and Dr V R. McReady.

This meeting will incorporate the 1988 **Silvanus Thompson Memorial Lecture**, which will be open to non-registrants.

**Radiobiology All-Day Non-topic Proffered Papers Meeting**
February 19, 1988
Organised by the Radiobiology Subcommittee

**New Demands on Diagnostic Equipment to Reduce Radiation Dose**
March 9, 1988
London, venue to be confirmed
All-day meeting organised by the Industry and Radiation Protection Committees.
Chairman: Dr J G. Russell

**Total-Body Irradiation**
April 13, 1988
Joint BIR/IPSM meeting organised by the BIR

**Conversazione**
June 23, 1988
Institute of Directors, London SW1

**BIR ties**

BIR ties are available to members at £5 each (£6 including post and packing) They are navy blue or maroon red and carry the rays from the Institute's logo, in gold. Please send a cheque payable to the BIR with the order.

**British Institute of Radiology 46th Annual Congress**
*incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting and in collaboration with the Scottish Radiological Society*

## Radiology '88

Glasgow May 23–25, 1988

Glasgow will be the first in a series of back-to-back meetings with the Annual Conference of the College of Radiographers. The technical exhibition will span both meetings and be the manufacturers' showcase in 1988

The place the brand new Scottish Exhibition and Conference Centre.

Radiology '88 will cover all aspects of radiology· X-ray diagnosis, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines.

Proffered papers and posters are invited closing date November 30 1987. Abstract forms available from BIR Conference office

**Hire of Institute facilities**

Readers are reminded of the availability for hire of the Lecture Theatre, Foyer and Library Affiliated societies are offered a discount.

The Lecture Theatre holds up to 100 people in raked seating and has excellent audio-visual equipment, including VHF video The Foyer provides space for registration and refreshment breaks for 40 people The Library, with its beautiful Adam ceiling, can accommodate up to 75 people for refreshment breaks or for an evening reception

**Members' use of the Toshiba Room**

Members may borrow the Toshiba Room free of charge, subject to availability This conference meeting room seats 16 people with comfort

Full details from Mrs Anne Clayton, Assistant Secretary, Administration at the BIR.

# Meetings and courses

*As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.*

**UMDS St Thomas' Hospital Medical School Postgraduate Centre Nuclear Medicine Biannual Intensive Course**
September 25–26, 1987
St Thomas' Hospital, London
Further details: Miss Erica Mendy, Postgraduate Secretary, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH (Tel. 01-928 9292 ext. 2072).

**The British Cervical Spine Society**
November 6–7, 1987
The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry
Further details: Mr A. Crockard, The National Hospitals for Nervous Diseases, Maida Vale, London W9 1TL. Tel: 01-286-5172.

**Duplex Imaging**
January 21–23, 1988
Hotel Inter-Continental, San Diego, California
Further details: Dawn Ryals, Ryals & Associates, P.O. Box 920113, Norcross GA 30092-0113. Tel: 404 641-9773.

**8th Annual Postgraduate Course—Uroradiology '88**
February 1–4, 1988
Stouffer Orlando Resort, Sea World, Orlando, Florida, U.S.A.
Further details: Dawn Ryals, Ryals & Associates, P.O. Box 920113, Norcross, GA 30092-0113. Tel: 404 641-9773.

**1st South African Medical Resonance Symposium combined with CT and Radiology Update**
February 12–13, 1988
University of Cape Town
Further details: Mrs S. Elliot, Postgraduate Medical Centre, UCT Medical School, Observatory 7925, Cape Town, South Africa.

**The Lyon Conference: Computer Science and Life. Medical Imaging and Specialist Systems applied to Medicine**
March 10–12, 1988
Ecole Normale Supérieure de Lyon, Lyon
Further details: Package, Les Entretiens de Lyon, 55 montée de Choulans, 69323 Lyon Cedex 05. Tel: 033 78 42 29 53. Telex: 330 295 F.

**International London Course in Whole Body Computed Tomography**
March 27–31, 1988
Gleneagles Hotel, Perthshire, Scotland
Further details: Mrs J. O'Donnell, Organising Secretary, Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, UK.

**7th International Congress of the International Radiation Protection Association (IRPA 7): Radiation Protection Practice**
April 10–17, 1988
Sydney, Australia
Further details: IRPA 7 Secretariat, GPO Box 2609, Sydney, NSW 2001, Australia (Tel: 02-241 1478, Telex AA74845 "Consec", Cable "Convention" Sydney).

**25th Congress European Society of Paediatric Radiology**
April 11–16, 1988
Montreux, Switzerland
Further details: Dr M. A. Hopf, 1 Route de Florissant, CH-1206 Geneva, Switzerland. Tel: 4122-47 25 47.

**Practical Interventional Radiology 1988**
April 25–28, 1988
The Lafayette Hotel, Boston, MA
Further details: Harvard Continuing Education, Boston, MA 02115. Tel: (617) 732-1525.

**11th International Congress of Head and Neck Radiology**
June 6–11, 1988
Uppsala, Sweden
Further details: H. Wilbrand, M.D., Department of Diagnostic Radiology, University Hospital, S-751 85 Uppsala.

**Annual Meeting and Postgraduate Course Arranged by the Cardiovascular and Interventional Radiological Society of Europe and the American Society of Cardiovascular and Interventional Radiology**
June 12–17, 1988
West Berlin.
Further details: Reingard Sörensen, M.D., Klinikum Steglitz, Röntgendiagnostik, Hindenburgdamm 30, 1000 Berlin 45, Federal Republic of Germany.

**2nd European Congress of NMR in Medicine and Biology**
June 23–25, 1988
International Congress Center, Berlin
Further details: Conference Secretariat, c/o Prof. Dr R. Felix. Department of Radiology, Charlottenburg University Hospital, Spandaeur Damm 130, D 1000 Berlin 19, Federal Republic of Germany.

**Australian Society for Ultrasound in Medicine 18th Annual Scientific Meeting**
September 1–3, 1988
Gold Coast, Queensland
Further details: Dr G. O'Brien, 225 Wickham Terrace, Brisbane, Queensland, 4000 Australia.

**European Joint Committee on Radiopharmaceuticals 3rd Postgraduate Course on Radiopharmacy for Clinicians**
October 17–22, 1988
Städtisches Klinikum Berlin Buch, DDR
Further details: Professor Dr H. Deckart, Städtisches Klinikum Berlin Buch, Nuklearmedizinische Klinik, DDR-1115.

**25th Congress of the Association for Medical Radiology in the DDR**
October 18–21, 1988
Symposium of CT and MR
October 17–18, 1988
Further details: MR Prof. Dr sc.med. M. Luning, Institut für Röntgendiagnostik, Schumanstr. 20/21 DDR, 1040 Berlin. Tel: 2 86 20 78.

**International Symposium on Magnetic Resonance Imaging**
December 14–16, 1988
New Delhi, India
Further details: Dr N. Prasad, Department of Radiology, Baylor College of Medicine, Houston, Texas 77030, U.S.A. Tel: (713) 799-4415.

# ANNA HAMANN SCHOLARSHIP PROGRAM

## for foreign students to study and train in the United States

The American Society for Therapeutic Radiology and Oncology Education and Development Fund is seeking candidates for the Anna Hamann Scholarship Program.

## Eligibility Rules

Each candidate must have completed at least two (2) years of specialised training in radiation oncology in a program outside the United States which is recognised by the board of directors of the American Society for Therapeutic Radiology and Oncology as providing suitable training in radiation oncology.

## Criteria for selection of Anna Hamann Scholars

1. Record of achievement in prior work in the field of radiation oncology, particularly as an indication of potential for making a significant contribution to the field.
2. Extent to which the particular professional goals of the candidate would be furthered by study and training in the United States.
3. Interest of the candidate in teaching or practicing radiation oncology in his or her country of origin or in another country other than the United States following the period of study and training as an Anna Hamann Scholar.
4. Financial need.
5. Availability to the candidate of similar training through programs other than the Anna Hamann Scholarship Program.

## Post-selection requirements for candidates

Before any portion of an Anna Hamann Scholarship grant may be paid to or on behalf of a qualified candidate selected by the board of directors, he or she must meet the following additional requirements:

1. Be accepted into a program of advanced training in radiation oncology in the United States which is acceptable to the board of directors of the American Society for Therapeutic Radiology and Oncology.
2. Satisfy the general requirements applicable to foreign physicians coming to the United States for postgraduate training, including passing the examination administered by the Educational Commission for Foreign Medical Graduates.
3. Obtain all required permission from appropriate immigration authorities to enter the United States and to remain in the United States for the period of time required to complete the designated course of postgraduate study and training.

To suggest a candidate or to request additional information, please contact William T. Moss, MD, Chairman, Department of Radiation Therapy, Oregon Health Sciences University, 3181 S.W. Sam Jackson Park Road, Portland, Oregon, 97201, U.S.A.

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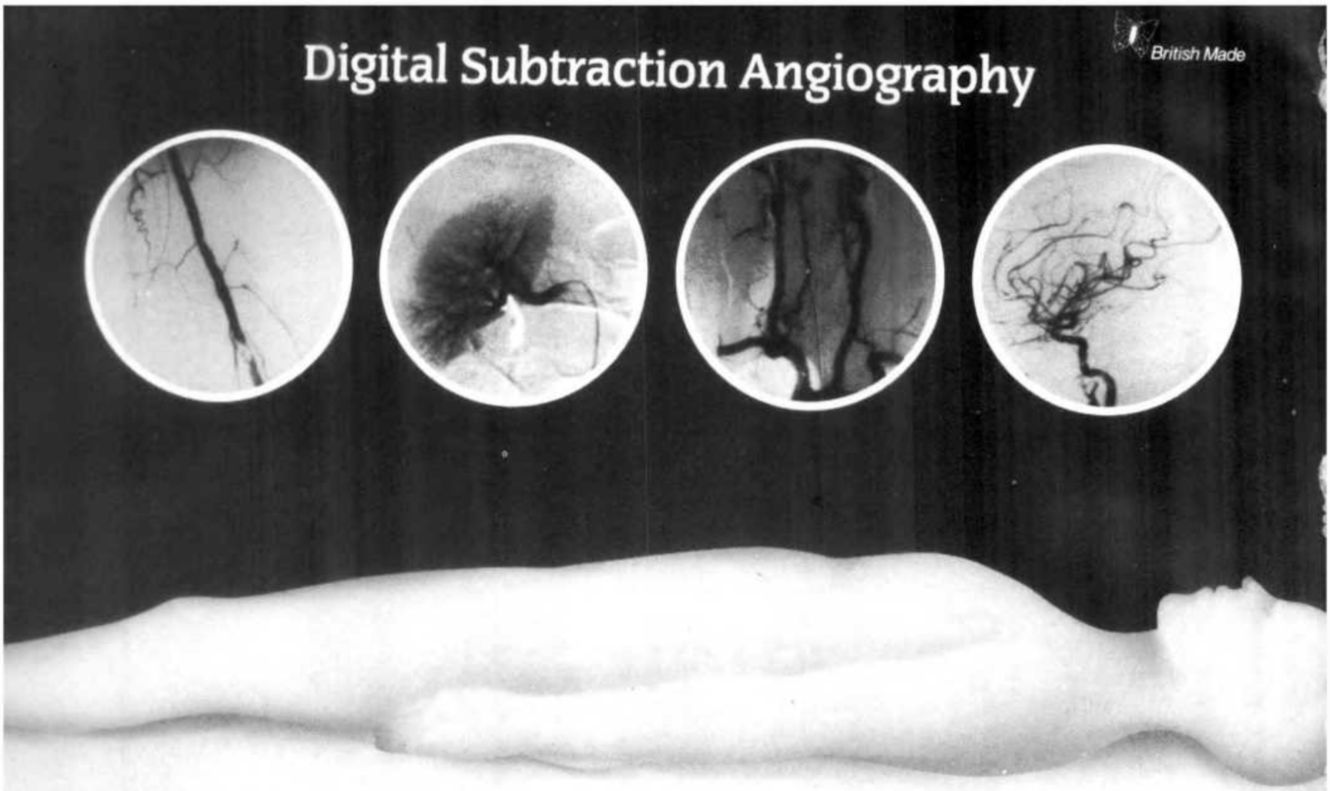

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